ARCHIVES OF SURGERY

VOLUME 34 JUNE 1937 NUMBER 6

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AUTOLYSIS OF TISSUE IN VIVO

AN EXPERIMENTAL STUDY WITH ITS CLINICAL APPLICATION IN THE PROBLEM OF TRAUMA TO THE LIVER

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In any consideration of tissue autolysis, which means the destructive changes which take place in tissues disconnected from their blood supply, one is immediately impressed by two facts. First, most of the previous discussions on the fatal outcome have centered around the part played by Bacillus Welchii, or the gas bacillus. Second, the problem has been regarded almost entirely as an experimental one. In only a few of the excellent contributions to the subject is there even a hint of a possible clinical application. We disagree with both of these points of view. Our own experimental work has led us to believe that the rôle of the gas bacillus in the fatal outcome is an entirely secondary one. Our experimental and clinical work on the so-called "liver death" has led us to believe that the problem has a clinical aspect which heretofore has been almost entirely overlooked.

The gas bacillus in relation to tissue autolysis first appears in a contribution by Jackson,[1] of the Harvard Medical School. In 1909, after he had become interested in previous work on this subject by Lane-Claypon and Schryver, he undertook a series of experiments to determine the initial physical and chemical changes in organs disconnected from their blood supply. Lane-Claypon and Schryver had noted three distinct periods in tissue autolysis, a latent period, a rapid period and a gradual period, and Jackson was particularly interested in the latent period. He was able to show that this period is more likely to be present when the tissues have been temporarily cooled or when the percentage concentration of inorganic salts (calcium and potassium) in them has been changed by the use of saline solution. He demonstrated

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1. Jackson, H. C.: Effect of Conditions upon Latent Period and Rate of Aseptic Post-Mortem Autolysis During First Ten Hours, J. Exper. Med. **11**:55-83 (Jan.) 1909.

that lipolytic and amylolytic changes are operative in autolysis just as much as proteolytic changes; indeed, the lactic and higher fatty acids, which are present as the result of amylolytic and lipolytic changes, augment the proteolytic autolysis. Furthermore, the longer the tissue autolysis continues, the more marked is the depression of the freezing point, which implies, in turn, the breaking up of the molecules into smaller divisions. Finally, and most important for our purposes, Jackson found that the depression of the freezing point was most marked when there was present in the tissues an organism which resembled no organism heretofore known. It was never present at the end of six or eight hours, but it was uniformly present after twelve hours in liver tissue which had been removed with aseptic precautions, ground, placed in saline solution and incubated at 38 C.

Later in the same year this new organism was studied by Wolbach and Saiki,[2] who found it in the livers and spleens of all but two of twenty-three dogs but present in the kidneys and spleen (which had been removed for comparative purposes) of only one dog. We need concern ourselves only with their gross descriptions. At the end of forty-eight hours they noted that the sterile livers were fairly firm and elastic, with their color and odor practically unchanged, and no gas was present. The livers containing the new bacillus were dark grayish green on exposure to the air and bright red in the areas in contact with the dish. Crepitation was marked. The consistency was soft and plastic, and there was a strong odor, not putrefactive but peculiarly rancid or fatty. After from twenty-four to forty-eight hours the closed end of the fermentation tube was almost filled with gas. Filtrates of these livers injected into the peritoneum or the mesenteric vein produced no clinical or postmortem changes in experimental animals. Because these bacilli were invariably present in the livers which showed autolytic changes in vitro and invariably absent in the livers which showed no such changes, the authors concluded that they were responsible for the production of gas, the discoloration and the characteristic odor noted in these experiments, and, by inference, were responsible for the autolysis which occurred. In the light of the views we hold on the subject, we may fairly say that these deductions got the subject of liver autolysis off to a bad start.

Still later in the same year Jackson [3] studied the sterile livers found in the experiments of Wolbach and Saiki and observed that after

2. Wolbach, S. B., and Saiki, T.: New Anaerobic Spore-Bearing Bacterium Commonly Present in Livers of Healthy Dogs, and Believed to Be Responsible for Many Changes Attributed to Aseptic Autolysis of Liver, J. M. Research **21**:267-275 (Sept.) 1909.

3. Jackson, H. C.: Concerning Question of Rate of Autolytic Reaction and Appearance of Gases and Acids in Autolysis of So-Called Sterile Livers of Dogs, J. M. Research **21**:281-284 (Sept.) 1909.

forty-eight hours the autolysis in them was comparable to the autolysis noted at the end of ten and twelve hours in the livers containing the new bacillus. This observation, in his opinion, further placed the responsibility for the autolysis on B. Welchii, as the organism was now called, and his conclusion, we believe, led later workers still further astray.

In 1927 Berg, Zau and Jobling [4] repeated the work of Jackson, Wolbach and Saiki. They found the organisms in the liver tissue of all of their animals, though they were not present in the blood of the portal vein or in the bile of the gallbladder, an observation previously made by Wolbach and Saiki. In 1930 [5] Gage showed that the organisms reached the liver by way of the alimentary canal, passing from the duodenum probably by way of the common duct. The bacilli found on culture of the hair of dogs and the breasts of nursing animals were identical with the bacilli found in the stomach of these animals and in the stomachs of the puppies.

The problem of liver autolysis attracted little attention until 1925, when Mason, Davidson, Matthew and Rastello [6] became interested in the use of heparin as an anticoagulant and sought some explanation of the widely varying reactions associated with its use. The method of its preparation suggested to them that liver autolysis might play some part in the results. It reminded them, too, of Mann's work, which showed that completely hepatectomized dogs lived longer than those with small amounts of liver substance free in the abdomen, and they sought to determine whether the autolysis in vivo of small amounts of liver tissue would liberate sufficient anticoagulant to be demonstrated by changes in blood coagulation. Their work stimulated further work on the subject, and since that time an elaborate series of experiments have been performed in various laboratories. These experiments, for purposes of clarity and convenience, we shall summarize in groups, under which we shall include the experiments which we ourselves have performed. Our comments and conclusions we shall reserve until later.

REVIEW OF EXPERIMENTS

1. *Implantation of Whole and Ground Liver.*—Mason and his associates, using fifteen dogs and employing the usual aseptic ritual, ligated one lobe of the host's liver and returned it free to the abdomen. All the animals were able to stand after operation and showed no signs of shock. Ten dogs died in from fifteen to eighteen hours, and none survived longer than seventy-two hours. Shortly before

4. Berg, B. N.; Zau, Z. D., and Jobling, J. W.: Bactericidal Function of Liver, Proc. Soc. Exper. Biol. & Med. **24**:433-434 (Feb.) 1927.

5. Gage, I. M.: Bacteriology of the Liver in Normal Dogs, Proc. Soc. Exper. Biol. & Med. **28**:257-259, 1930.

6. Mason, E. C.: Note on Use of Heparin in Blood Transfusion, J. Lab. & Clin. Med. **10**:203-207 (Nov.) 1924. Mason, E. C.; Davidson, E. C.; Matthew, C. W., and Rastello, P. B.: Study of Tissue Autolysis in Vivo: I. Blood Changes; Physical and Chemical, ibid. **10**:622-630 (May) 1925.

death, and with little warning, each animal turned on its side, with all four legs extended, respiration became labored, and death followed soon, with no struggle except the terminal one suggesting air hunger. Studies of the blood during life showed no significant changes in plasma volume, serum volume, fibrin, blood coagulation, amino-acids, sugar, urea nitrogen or uric acid.

The observations at postmortem examinations were invariably the same. The abdominal cavity contained from 100 to 300 cc. of brownish fluid, which was not actually blood. There was a pseudofibrinous exudate, which was easily removed. The intestines were markedly hyperemic and congested, as was the omentum, which was wrapped around the free liver. This liver tissue showed no gross characteristics of its origin. It was light chocolate in color and so spongy and crepitant that it had almost the feel of lung tissue. The ligated sections, which had weighed from 30 to 110 Gm. on implantation, had lost from 6 to 40 Gm. each.

Mason's experiments have since been repeated by Wangensteen and Waldron [7] in the course of a series of experiments on the toxicity of various tissues autolyzed in vivo; by Haden and Orr [8] in the course of a study of blood chlorides in proteose intoxication, and by Ellis and Dragstedt.[9] The longest period of survival was that of a dog used by Wangensteen and Waldron, which lived for five days, and all the experimental work duplicated that of Mason. Ellis and Dragstedt, in addition to implanting the liver within the abdomen, also implanted it in the abdominal wall; a subcutaneous abscess developed, but the animal survived. Mason and Lemon,[10] in similar experiments, endeavored to keep the animals alive by forcing fluids by various routes and by draining the peritoneal cavity. None of the animals survived longer than nineteen hours and twenty-five minutes, and the promptest death, in twelve hours and forty-five minutes, was that of the animal in which peritoneal drainage was done.

We repeated all of these experiments, using both whole and ground livers, always from other animals, for intraperitoneal implantation. All the animals died in from eight and a half to sixteen hours and presented the characteristic postmortem changes.

2. *Implantation of Preheated Liver.*—Ellis and Dragstedt preheated the liver before intraperitoneal implantation to a temperature of from 75 to 80 C. for from fifteen to twenty minutes in an endeavor to destroy the autolytic enzymes. At the end of this period they were still able to culture positive anaerobic organisms from the tissues; death occurred from autolytic peritonitis in from twenty-four to thirty-six hours after implantation and the same organism was cultured after death. Dvorak [11] could not produce death by the use of simple boiled liver, though it invariably occurred if the liver was first incubated.

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7. Wangensteen, O. H., and Waldron, G. W.: Studies in Intestinal Obstruction: IV. Strangulation Obstruction; Comparison of Toxicity of Intestine and Other Tissues Autolyzed in Vivo and in Vitro, Arch. Surg. **17**:430-439 (Sept.) 1928.

8. Haden, R. L., and Orr, T. G.: Blood Chlorides in Proteose Intoxication, J. Exper. Med. **48**:639-645 (Nov.) 1928.

9. Ellis, J. C., and Dragstedt, L. R.: Liver Autolysis in Vivo, Arch. Surg. **20**:8-16 (Jan.) 1930.

10. Mason, E. C., and Lemon, C. W.: Anhydremia as Possible Cause of Deaths in Liver Autolysis, Surg., Gynec. & Obst. **55**:427-431 (Oct.) 1932.

11. Dvorak, H. J.: Liver Autolysis in Peritoneal Cavity of Dog, Proc. Soc. Exper. Biol. & Med. **24**:431-434 (Jan.) 1932.

Repeating these experiments, we preheated the liver before implantation at a temperature of from 75 to 80 C. for two hours. All the dogs died in from forty to forty-five hours. We did not culture the livers before implantation, unfortunately, but we did recover the organisms postoperatively, and we noted the usual postmortem changes.

3. *Implantation of Autoclaved and of Incubated Liver.*—Ellis and Dragstedt autoclaved liver at a pressure of 15 pounds (6.8 Kg.) for fifteen minutes, after which they could not recover the organism, nor did death follow the implantation of these tissues. Dvorak added autoclaved liver to filtrates of incubated ground liver, and his dogs also survived. Andrews and Hrdina[12] implanted autoclaved liver, which had been proved sterile, in six dogs. Four died of autolytic peritonitis in from eighteen to seventy-two hours. One animal, killed in seventeen days, showed the implanted liver scattered throughout the abdomen and partially absorbed. Trusler, Reeves and Martin[13] implanted finely ground autoclaved liver in seven dogs; one died of autolytic peritonitis in fifteen hours and another in eighteen hours; in the latter animal the implantation had been made in the abdominal wall through error. Another dog died of pneumonia in eleven days, but all the others survived. Dvorak's experiments also showed that autoclaved ground liver was not lethal. Andrews and Hrdina, who used autoclaved liver in a dog with jaundice and in another with a biliary fistula, produced autolytic peritonitis, but their results may perhaps be discounted in view of the preexisting pathologic process. Ellis and Dragstedt reinfected sterile autoclaved livers with organisms isolated in pure culture from fresh livers and invariably caused death in twenty-four hours, whether the implantation was done in the peritoneal cavity or in the abdominal wall.

In one of our experiments with unground autoclaved liver the animal died of autolytic peritonitis at the end of twenty-six hours, and the gas bacillus was recovered from the abdominal fluid. The other animals lived, whether ground or whole liver was implanted.

Andrews and Hrdina, and Trusler, Reeves and Martin, in various experiments with autoclaved, incubated liver, produced death in varying lengths of time, rarely over seventy-two hours, and typical postmortem changes were observed, though Trusler and his associates, in their elaborate bacteriologic studies, were not consistently able to obtain B. Welchii on culture. One dog in their series lived as long as six weeks, and then, as happens in the best of laboratories, was accidentally cremated before it could be examined.

Using 150 Gm. of ground, incubated liver, we produced autolytic peritonitis with death in nine hours. When the same amount of ground, incubated liver was autoclaved before implantation, death was deferred for thirty-six hours.

4. *Implantation of Various Sections of Liver.*—Mason and Nau,[14] conceiving the idea that the exact section of liver implanted might alter the result, implanted the peripheral portion in a rabbit. When the animal was killed after sixty-seven hours no gas was present, but there was noted a small amount of free fluid in the

12. Andrews, E., and Hrdina, L.: The Cause of Death in Liver Autolysis, Surg., Gynec. & Obst. **52**:61-66 (Jan.) 1931.

13. Trusler, H. M.; Reeves, J. R., and Martin, H. E.: Significance of Anaerobic Organisms in Peritonitis Due to Liver Autolysis, Arch. Surg. **30**:371-393 (March) 1935.

14. Mason, E. C., and Nau, C. A.: The Cause of Death Due to Liver Autolysis, Surg., Gynec. & Obst. **60**:769-774 (April) 1935.

abdomen, together with fatty degeneration of the liver, septic cholangeitis and toxic parenchymatous degeneration of the kidneys. When the central portion of the liver was implanted, the rabbit died suddenly at the end of twenty-six hours, and the gas bacillus was cultured from the implanted liver.

We repeated these experiments with dogs. Whether the central or the peripheral portion of the liver was used, death occurred within eighteen hours from autolytic peritonitis, and B. Welchii was recovered from the peritoneal fluid.

5. *Implantation of Tissues Other Than the Liver.*—Using tissues other than the liver, we found that death occurred in twenty-six hours after implantation of the pancreas, in thirty-one hours after implantation of the heart with its valvular and vascular apparatus, in thirty-six hours after implantation of the lung and of the spleen and in forty-eight hours after implantation of the kidney. The only animal which survived was one in which only the heart muscle was implanted. It is worth mentioning that the animal which died the most promptly, the one in which the pancreas was implanted, was the only one on its feet the morning after operation, and its temperature, checked with three different thermometers, was 94 F., the lowest reading possible, four hours ante mortem.

Wangensteen and Waldron implanted various organs other than the liver, death occurring in a large proportion of the animals. They implanted the kidney in three dogs, with one death, and the spleen in twelve dogs, with eight deaths in an average of three and one-half days. Mason and his associates [15] implanted the spleen in six dogs, with three deaths in from thirty-six to forty-five hours. No investigators, so far as we can determine, have used the lung or the heart except ourselves.

6. *Intraperitoneal and Intravenous Injection of Various Liver Extracts.*—Andrews and Hrdina injected intraperitoneally a concentrated extract of incubated liver, and death occurred in from seven to eighteen hours from autolytic peritonitis, although the same experiment with a less concentrated extract produced no perceptible effect. Our results from the intraperitoneal and the intravenous injection of liver extract, no matter what the degree of concentration and no matter whether or not the liver had been previously incubated, were all negative. Our conclusions are the same as those of Dvorak, i. e., that injections of aqueous extracts of ground, incubated liver that have been boiled are not fatal, nor are injections of ether or alcohol extracts of ground fresh liver. Dvorak's conclusion that the extract of incubated liver is fatal is in accordance with Andrews' results, but not with our own.

We lay no great stress on experiments with liver extracts. Any variation in preparation and concentration may result in a wide variation in results, and unless uniformity of preparation is certain, conclusions drawn from such experiments can only cloud the issue. For the same reason we are discarding the extensive experiments of Wangensteen and Waldron with various extracts in rats. It may be said, however, that in their work death occurred promptly in most cases, the brevity of survival being in inverse proportion to the length of incubation. The only rat which lived received a smaller dose than the others, and the extract was prepared after a much shorter period of incubation.

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15. Mason, E. C.; Davidson, E. C., and Matthew, C. W.: Study of Tissue Autolysis in Vivo: III. Observations Using the Spleen, J. Lab. & Clin. Med. **10**:997-999 (Aug.) 1925.

As early as 1925 Mason and his associates [16] injected intravenously an extract of liver autolyzed in vivo and produced variations of a temporary character in the heart rate and blood pressure, even when pithed animals were used. Mason and Nau worked with rabbits. One showed no ill effects from the injection. The other was killed in five minutes and placed in the incubator for twenty-two hours. At the end of this time all the tissues were crepitant, and gas bacilli were cultured from the host's liver.

7. *Intraperitoneal and Intravenous Injection of the Peritoneal Exudate of Dogs Dying from Autolytic Peritonitis.*—Andrews, Rewbridge and Hrdina [17] injected intravenously various fractions of the peritoneal exudate of dogs dying of autolytic peritonitis, without ill effect. On another occasion they introduced intravenously 240 cc. of the peritoneal exudate of a dog which had just died of autolytic peritonitis, again without ill effect.

We duplicated these experiments, with similar negative results. We also introduced intraperitoneally the entire peritoneal exudate of a dog which had just died of autolytic peritonitis, the animal surviving and seeming to be unaffected by the dose.

8. *Implantation of Various Culture Mediums and Bacterial Suspensions.*—We implanted in the peritoneal cavity of experimental animals both agar and sterile brain broth without effect. We also implanted anaerobic suspensions cultured from the peritoneal cavities of dogs in which various tissues had been implanted and death had occurred from autolytic peritonitis, again without effect. When anaerobic and aerobic suspensions from the same source were implanted, or aerobic suspensions alone, death followed within eighteen hours, although the picture was definitely not that of autolytic peritonitis. Streptococci, in some instances combined with staphylococci, and colon bacilli were regularly recovered from the peritoneal exudate. Dvorak produced death by the intraperitoneal implantation of an anaerobic suspension, although no results followed when the material was boiled before implantation. He noted also that death could be produced by the implantation of sublethal amounts of the bacterial suspension to which autoclaved ground liver had been added. Andrews and Hrdina made cultures of Welch bacilli from the peritoneum of dogs which died of autolytic peritonitis and injected the suspension into normal animals. The animals showed no reaction, and the peritoneal cavity was sterile when the four dogs were killed at the end of four days.

To show that the mere introduction of foreign substances has no deleterious effect, we introduced into the peritoneal cavity through a puncture wound 60 cc. of citrated blood from the animal's own femoral vein. No results of any sort were noted.

9. *Implantation of Fetal Liver.*—In 1930 Ellis and Dragstedt implanted in the peritoneal cavity fetal liver secured at cesarean section. In one animal only the liver was implanted; in another the entire abdominal viscera were added, and in the third the liver of a puppy which was infiltrated with a pure culture of anaerobic organisms was implanted. All the dogs remained well. When the abdomens of the animals were reopened at the end of twenty-six days there was no trace of the implanted liver in two of the dogs. In the third there was an intraperitoneal abscess containing pus from which anaerobic bacilli could be cultured, although

16. Mason, E. C.; Davidson, E. C., and Rastello, P. B.: Study of Tissue Autolysis in Vivo: II. Pharmacological Study of Toxic Material, J. Lab. & Clin. Med. **10**:906-913 (July) 1925.

17. Andrews, E.; Rewbridge, A. G., and Hrdina, L.: Causation of Bacillus Welchii Infections in Dogs by Injection of Sterile Liver Extracts or Bile Salts, Surg., Gynec. & Obst. **53**:176-181 (Aug.) 1931.

there was no trace of the implanted liver. Their conclusion was that the autolysis of sterile liver in vivo is not fatal.

We performed three experiments with fetal liver. In the first dog we implanted the livers of two puppies (35 Gm.) secured at cesarean section, and in the second dog we implanted the livers of four puppies (70 Gm.) secured at the same section. The first dog showed no effect of any sort. The second dog looked very ill for several days, then gradually recovered and remained well. In a third dog we implanted the livers of ten puppies (150 Gm.) secured at a single cesarean section. The dog got to its feet shortly after operation but was perceptibly droopy at the end of eighteen hours; it died three hours later, rather sooner than we anticipated. At autopsy the pathologic changes were typical of those due to autolytic peritonitis.

10. *Unduplicated Experiment.*—Using six dogs and implanting variously unground unautoclaved liver, unground autoclaved liver, ground unautoclaved liver and ground autoclaved liver, we also injected gas bacillus antitoxin into the animals, using it intraperitoneally, intramuscularly, intravenously or in a combination of these methods. Five of the animals died in from fifteen to forty hours, and on postmortem examination the pathologic changes were typical of those due to autolytic peritonitis. The sixth dog survived; 125 Gm. of unground, autoclaved liver had been implanted and 20 cc. of gas bacillus antitoxin injected intravenously. After being ill for several days, the dog seemed to recover completely. When its abdomen was reopened twenty days later there was no evidence whatever of a peritoneal reaction. The transplanted liver, which was completely encapsulated by omentum, was in excellent condition. It was our intention to reimplant it into another dog, but the laboratory porter, in an entirely atypical burst of cleanliness, threw it away with the sterile gauze in which it had been placed, and the plan could not be carried out. The host died some time later of natural causes.

COMMENT

This concludes, then, our own experiments and the more important of the previous experiments on tissue autolysis. What conclusions can be drawn from them? Before that point is discussed, one or two other facts should be emphasized. In the first place, we used dogs throughout, and our experimental work, therefore, has a sameness of background, as it were, which is disturbed in the experiments of others, it seems to us, by the occasional use of rabbits, guinea-pigs and rats as well as dogs. In the second place, our sterile technic was as flawless as we could make it, and we were careful in our last experiments to follow the plan of Trusler and his associates and hold the edges of the wound open as the liver was implanted. This method eliminates any possibility of contamination from the tissues of the abdominal wall, to which these workers are inclined to attribute the presence of the gas bacillus.

More important than these facts is the fact that the postmortem observations made in our experiments differ in one respect from those made by many other observers. We found, as they did, serosanguineous fluid in the abdominal cavity and congestion and hyperemia of the peritoneal surfaces, the intestinal tract and the omentum, which practically always encapsulated the implanted liver. We found, as they did, that the implanted liver had changed its form and appearance and had become

friable, gray and necrotic. But the change in the host's liver, especially stressed by Andrews and Hrdina, we noted only in cases *in which autopsy was delayed.* The observations of these authors in regard to the host's liver include gaseous crepitation, friability, a greasy feel and microscopic degeneration and necrosis, suggesting the picture of a severe toxic reaction rather than of a severe infection. When autopsy was delayed, as we have said, and particularly when it was delayed in hot weather, we noted these pathologic changes. When autopsy was done immediately, the host's liver was sometimes, though not always, congested and hyperemic, but it was never crepitant, friable or greasy, nor did it show marked microscopic evidence of degeneration. Earlier in the communication of Andrews and Hrdina occurs this statement: "In the vast majority of cases when the intraperitoneal injections or implantations were made in the afternoon, the animal was found dead and cold at 8 o'clock in the morning." This suggests that in this series, as well as in others in which their observations were duplicated, autopsy was delayed. It is our practice in experimental work to spend the night in the laboratory and to observe our animals at hourly intervals, remaining constantly with them if they seem on the point of death, so that autopsy is not delayed. We emphasize this point especially, for in other experimental work in which autolysis could play no part we have noted, whenever autopsy was delayed, the postmortem changes in the liver described by Andrews and Hrdina. Furthermore, we believe that the inconsistent findings of gas in the peritoneal cavity which are reported in various clinics can also be explained by delay in autopsy. When we opened the abdomen immediately after death, we never found gas, and only when unautoclaved or incubated liver had been used did we note the foul odor usually associated with the gas bacillus. When autopsy was delayed, gas was present, and associated with it always was the distinctive foul odor of the gas bacillus.

If the reports of the various experiments which we have summarized are carefully read, certain generally consistent results will be noted. It will be observed that when whole liver or ground liver was implanted, death followed rather speedily, especially when ground liver was used. This is true whether the liver was secured from the host itself or from another animal, in which case the factors of trauma, hemorrhage and shock naturally present in auto-implantation are entirely eliminated. It will be noted that death occurred at a longer interval when the implanted liver was first autoclaved and at a shorter interval when the implanted liver was first incubated. All of the animals which survived were animals in which autoclaved liver was implanted. It will be noted that death occurred regardless of what portion of the liver was

used. It will be noted that death occurred almost uniformly whether the liver or other tissues were used. We have already noted the variable results with liver extracts, and we think we may fairly refrain from further discussion of that point. It will be noted that in our own experiments, which were partially duplicated by other workers, death did not follow the implantation of anaerobic suspensions. It will be noted that the intravenous and the intraperitoneal injection of the peritoneal exudate of dogs which died of autolytic peritonitis caused no ill effects. It will be noted that our experiments with the implantation of fetal liver did not duplicate the experiments of Dragstedt and Ellis, in which the animals survived. It will be noted, finally, that in our experiments with implanted liver in which we used gas bacillus antitoxin in various doses and by various routes all but one of the animals died.

How are these conflicting results to be explained? Quite simply, it seems to us. In the first place, let us dispose of certain factors operative not only here but in other conditions. We noted, for one thing, that the resistance of the animal played some part, though not an important one, in the outcome. An animal which had been fed under our direction in our own animal house for several days before operation usually lived longer—and sometimes even survived—than an animal brought in from the street and operated on at once. This factor, however, we mention only tentatively, for too many other circumstances were associated to make it possible to advance it as an important consideration.

Again, the loss of blood volume resulting from the presence of free fluid in the peritoneal cavity, from the hemorrhagic infiltration of the omentum surrounding the implanted tissue and from the hyperemic and hemorrhagic changes in the mesentery and intestinal tract plays some part in the fatal outcome. These changes would be important under other circumstances, though here, again, other factors confuse the picture. The suddenness of death in these cases is very striking. The animal is up and moving about, apparently quite well. An hour or two later it is on its side, obviously very ill. A few minutes later it may be dead.

But these are minor considerations, and we mention them chiefly to eliminate them. They do not explain what happens in these experiments. That explanation lies along other lines. Previous investigators are of two opposite schools of thought. One school, represented by Ellis and Dragstedt, believes that the important consideration is the growth of bacteria in the autolyzing liver or other tissues. As Dragstedt [18] pointed out to us in a personal communication, he is not con-

18. Dragstedt, L. R.: Personal communication to the authors.

vinced that "in the absence of bacterial growth in the necrotic tissue a toxemia can result." The other school of thought is represented by Andrews and his co-workers, who, curiously, are in the department of surgery at the University of Chicago, as is Dragstedt. Their conclusion is that in such cases "death is not due to a generalized peritonitis but rather to the absorption of toxic products generated from the liver tissue deprived of its circulation," and they have cited, in support of their idea, their experiments which show that the anaerobic bacilli found at the time of death may be injected intraperitoneally and intravenously without causing any harmful results.

All the experimental work that has been done, it seems to us, both in our own laboratory and elsewhere, points to the correctness of the latter point of view. We noted in our own experiments that death followed more quickly when ground liver was used than when unground liver was implanted. We noted that death followed more quickly when incubated liver was used than when unincubated liver was used. We noted that when autoclaved liver was used death was postponed and sometimes did not occur at all. Our conclusion from these observations is that while autolysis can occur under any circumstances with the implantation of liver, the latent period is prolonged by the use of autoclaved liver, sometimes so prolonged that the animal actually acquires a tolerance, as it were, and is thus able to escape death. When incubated liver is used, on the other hand, death is hastened, because the latent period is shortened or even eliminated, depending on the length of the incubation.

When whole, unground liver was used, death always occurred after a longer interval than when ground liver was used, and this also seems reasonable. Laying aside the possibility of cellular destruction and the faster liberation of autolytic enzymes, both of which are likely to occur when the liver is ground, it is logical to assume that the rate of autolysis and the consequent absorption of toxins will be faster because of the larger surface area. When the liver is used in a single piece, temperature changes occur more slowly, and disintegration of the outer surface must occur before the destructive process can extend inward, with the logical result that the absorption of toxins is retarded and death is deferred.

We noted almost invariably in our own experiments, though adequate data were missing for us to make the comparison with the reported experiments of others, that there was a definite relationship between the size of the dog and the amount of implanted liver. A small dose in a large dog meant a longer duration of life than the same dose in a smaller dog. An animal in which 100 Gm. of liver was implanted, for instance, lived sixteen hours, whereas an animal of the same size in which 150 Gm. was implanted died in eight and one-half hours.

This relationship was always definite and unmistakable, and it is most perfectly exemplified in our experiments with fetal liver. All three hosts were approximately the same size and weight. When a small amount of liver (35 Gm.) was implanted, there was no perceptible effect. When a larger amount (70 Gm.) was implanted, the animal was obviously ill but was able to take care of the toxemia. When a still larger amount was used (150 Gm., the amount used in most of our other experiments), the result was exactly as it was when adult liver was implanted, a quick death with a typical picture of autolytic peritonitis.

The fatal effect of the implantation of tissues other than the liver can be explained by exactly the same reasoning we have just set forth. It is significant that the only animal which survived in this particular series of experiments was a large dog in which only the heart muscle (75 Gm.) was implanted. When the heart was implanted with its vascular and valvular supply (100 Gm.), death followed quickly.

Our own idea of the rôle of the gas bacillus in autolytic peritonitis is that it is entirely secondary. Of its importance there can be no question. It is impossible to eliminate it entirely. But it is the autolysis, in our opinion, which produces the fatal results, and not the presence of the gas bacillus. This is proved conclusively, first of all, by our experiments with autoclaved liver and by the experiments of others. Some of the dogs lived, but some of them died. If the elimination of the gas bacillus were the important factor most investigators believe it to be, all of the dogs should have lived, and all of them did not, either in our own series or in any other series. The fact that autolysis occurs less speedily after autoclaving the liver and more speedily after incubating it we explain by the duration of the latent period, which is prolonged in the first instance and shortened or eliminated in the second, rather than by the presence or absence of the gas bacillus. It should be remembered, in this connection, that whenever the peritoneal fluid was cultured after death, whether the autolytic peritonitis had been produced by autoclaved or nonautoclaved liver, the anaerobic organism was present. Yet the injection of this fluid, intravenously or intraperitoneally, did not reproduce the pathologic change, which it should have done, it seems to us, if the rôle of the organism were as important as it is assumed to be. It must be remembered, furthermore, that we were unable to reproduce autolytic peritonitis by the intraperitoneal injection of anaerobic suspensions. In Andrews and Hrdina's similar experiment, just as in ours, the peritoneal cavity was always sterile after death; it should not have been if the gas bacillus has the potency it is supposed to have.

Our own experiments show that the use of gas bacillus antitoxin cannot stave off the fatal outcome in autolytic peritonitis, regardless of the method of administration or of the dosage used. The single animal which survived in our series was a large dog, in excellent condition, in which 75 Gm. of autoclaved liver was implanted in a single piece. All the circumstances were favorable: a large dose, a small amount of implanted liver, good resistance, slow absorption because of the smaller surface area and a longer latent period because of the previous autoclaving. The use of the gas bacillus antitoxin had little or nothing to do with his survival, we are sure. The circumstances for survival were simply more favorable than in the other dogs in this group. The results with gas bacillus antitoxin are so uneven that this argument is another one we use only tentatively, but it does seem that if the gas bacillus itself were at fault the use of the antitoxin might have showed results in one or two animals.

The most important proof of the whole matter, to us, lies in our experiments with fetal liver. Clearly, as we have pointed out, it was the amount injected in those experiments which made the difference. The livers were all sterile, and all were secured and implanted with hyperaseptic precautions. The animals were all the same size and in the same condition. Only the amount of implanted liver was the variable factor. When a small amount was implanted, there was no result. When a larger amount was implanted, there was a perceptible though not a lethal effect. When a still larger amount was implanted, the animal died of autolytic peritonitis. Ellis and Dragstedt's own experiments, for that matter, go to prove our point. If the tissue autolysis is bacterial, why did not the animal die in which they implanted a fetal liver infected with a culture of B. Welchii? The explanation of their negative results, in our opinion, is not the absence of bacteria but the small amount of liver implanted. We do not know the size of their experimental animals, but we do know that a fetal liver, even when all the abdominal viscera are added, weighs very little.

Our own idea is that the presence of the gas bacillus in tissue autolysis is important only in that it hastens the process of autolysis by acting as a catalyst. Its absence, whether achieved by autoclaving or occurring normally, slows up the process by prolonging the latent period, sometimes to such a degree that the animal is able to survive. Incubation has the reverse effect; by increasing the activity and the number of the organisms, it hastens or eliminates the latent period, and death follows quickly. This theory is supported by Jackson's original observation, the significance of which has either been entirely overlooked or incorrectly interpreted. He noted in his experiments on tissue autolysis that when the gas bacillus was present there was a more rapid depression of the freezing point, a process which is dependent on and

coupled with the rate of formation of the more simple protein molecules. He noted further that when the gas bacillus was present, the rate of autolysis at the end of ten and twelve hours was comparable to the rate of autolysis after forty-eight hours when it was not present. The clue to the problem has been at hand all these years, we believe, but it has been overlooked up to this time.

CLINICAL CONSIDERATION

Turning to the clinical aspects of the problem, we note that for some time there has been an endeavor to associate the gas bacillus as an etiologic agent with such clinicopathologic states as intestinal obstruction, acute appendicitis and trauma of various sorts, though so far most uneven results have followed the use of gas bacillus antitoxin. We wonder whether in those states the important consideration is not tissue autolysis rather than the gas bacillus antitoxin. Gangrene of the appendix involves tissue autolysis. Strangulation obstruction and subsequent gangrene involve tissue autolysis. Trauma to tissue involves tissue autolysis. Is it not likely, in all of these states, that the emphasis has been placed on the wrong thing? Is it not likely that the toxemia associated with them is due primarily to the presence of tissue disconnected from its blood supply and undergoing autolysis rather than to the presence of the gas bacillus? If our theory is correct, the uneven and unsatisfactory results of gas bacillus antitoxin are easily explained; it can have no effect on a toxemia produced by the autolysis of tissues.

These pathologic states have been considered by other observers, however, even if not exactly as we have considered them. We desire to turn our attention now to another clinical problem which so far has been entirely overlooked, the significance of tissue autolysis in cases in which the liver has been subjected to trauma.

Not with the idea of making a statistical report but solely from this aspect we have studied the records of patients with injury to the liver who were treated at the Charity Hospital in New Orleans for the last ten years. There were ninety-eight cases in all, with sixty deaths. In only fifty-four cases, however, with twenty-six deaths, a mortality of 48.1 per cent, was the liver alone involved, and the other cases we have eliminated from our discussion. The damage to the liver in them may have played a part, perhaps an important part, in the morbidity and mortality, but since injuries to other structures complicated the picture, we have preferred to analyze only the cases in which trauma to the liver alone was responsible for what happened.

In the whole group of fifty-four cases, thirty-nine injuries followed gunshot wounds, with eighteen fatalities; seven were due to stab wounds, with one fatality, and eight were due to rupture, with seven fatalities

Obviously stab wounds of the liver are the least fatal form of injury, and ruptured wounds the most dangerous, which is entirely in accord with our theory that the actual destruction of the liver tissue plays a much larger part in these cases than is generally realized.

While it has nothing to do with our point, it may be of interest to note that, as usually happens in this community, most of these patients were Negroes. The thirteen white patients, two of whom were females, were usually innocent by-standers or innocent victims of accidents. The Negroes, twenty-nine of whom were males, furnished, as always, the bulk of the patients. Oberhelman and LeCount,[19] in a study of gunshot wounds, mentioned the contribution of American surgeons to this problem and particularly the contributions of Southern surgeons, who have always had the Negroes on their doorsteps. On the other hand, with the increasing use of automobiles and of heavy modern machinery, crushing injuries of the abdomen are increasing in number and need to be seriously considered.

Wounds of the liver are always serious. According to Vance's [20] figures, 33.3 per cent of such injuries are immediately fatal from shock and hemorrhage. Another 38 per cent result fatally within six hours, and treatment is impossible. In his series only 28.6 per cent of the patients lived long enough for clinical observation, and of these only 10 per cent were in shape for surgical treatment, which means, if the figures are generally applicable, that 90 per cent of such patients die before the surgeon has any chance to save them. According to Robertson,[21] at the Guthrie Clinic no patient with a severe injury to the liver has lived long enough to be taken to the operating room.

Of eleven patients treated conservatively at the Charity Hospital, the diagnosis of trauma to the liver was only presumptive for the four who survived. The history and clinical course suggested damage to the liver, but it could not be proved. In the seven patients, or 63.6 per cent, who died, the diagnosis was proved by postmortem examination at the coroner's office, where, unfortunately, autopsy is performed in most of these cases, which prevents the intimate observation that this subject, in our opinion, gravely needs. In the forty-three cases in which operation was done, with nineteen deaths, a mortality of 44.2 per cent, the diagnosis was proved both by operation and by autopsy.

Of the patients who lived, eight were treated by suture of the liver, against none in the group who died. One patient was treated by suture

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19. Oberhelman, H. A., and LeCount, E. R.: Peace Time Bullet Wounds of the Abdomen, Arch. Surg. **32**:373-412 (March) 1936.

20. Vance, B. M.: Subcutaneous Injuries of Viscera: Anatomic and Clinical Characteristics, Arch. Surg. **16**:631-679 (March) 1928.

21. Robertson, H.: Visceral Wounds Due to Trauma Where Abdominal Wall Has not Been Perforated, Am. J. Surg. **14**:395-418 (Nov.) 1931.

with muscle, against two in the group who died. Seven patients in the group who lived were treated by simple exploration, against three in the group who died; in the former group nothing more was done because it was not considered that anything more was needed, and the decision was correct; in the latter group, that decision was clearly in error in two cases, while in the third case nothing was done as a matter of necessity, it being impossible to check the bleeding by any method. In three patients in the group who lived and in four in the group who died it was impossible to tell what had been done; our conclusion is that no surgical treatment was attempted, for the reasons we have just set forth. Finally, in a double injury in a fatal case, both suture and pack were resorted to. It is perhaps of significance, even though the series is too small to draw conclusions from, that eight patients on whom suture of the liver was performed recovered, while the method was not employed on a single patient who died.

In the fatal cases in which surgical treatment was employed the causes of death included peritonitis in three, in two of which pneumonia was a factor; shock and hemorrhage in six; pneumonia in one; infection with gas bacilli, probably introduced with the bullet, in one; sepsis in one, and what we term "liver death" in seven, in one of which hemorrhage was also a factor.

We have been interested in collecting from the literature reports of the so-called liver death after trauma to the liver. The first case was reported by Furtwaengler [22] in 1927, from Clairmont's Clinic in Zurich. The second was reported by Stanton [23] in 1930. The third was reported by Helwig and Orr [24] in 1932. Autopsy was not performed in Stanton's case but was performed in the two cases reported by the other authors, and in each there was found, in addition to a traumatic necrosis of the liver, a high grade bilateral necrosis of the cortex of the kidneys.

In the cases which we are reporting, six of which we have previously reported,[25] autopsy in the hospital was permitted in only two cases, in each of which the liver had ruptured. In the other cases, however, the clinical course was absolutely typical of the liver-kidney syndrome, the axillary temperature rising to from 105.4 to 108.2 F. In two cases the surgeon's notes mention the high grade necrosis of the

22. Furtwaengler, A.: Diffuse Rindennekrose beider Nieren nach Leberruptur, Krankheitsforschung **4**:349-374, 1927.

23. Stanton, E. M.: Immediate Causes of Death Following Operations on Gallbladder and Ducts, Am. J. Surg. **8**:1026 (May) 1930.

24. Helwig, F., and Orr, T. G.: Traumatic Necrosis of the Liver with Extensive Retention of Creatinine and High Grade Nephrosis, Arch. Surg. **24**:136-144 (Jan.) 1932.

25. Boyce, F. F., and McFetridge, E. M.: So-Called "Liver Death": A Clinical and Experimental Study, Arch. Surg. **31**:105-136 (July) 1935.

liver found at operation, and in a third case, in which operation was done six days after the injury, it was specifically stated that there was no trace of peritonitis at the time. By presumption, it seems to us, these cases can fairly be classified as examples of "liver death."

In each case of rupture of the liver immediate exploration was done. The clinical course was at first smooth, but later uremic symptoms were apparent. In one case profound jaundice followed, the icteric index reaching 210. Autopsy in each case revealed typical degenerative changes within the liver and kidneys, in one instance so extensive as to suggest acute yellow atrophy.

We believe that this syndrome explains the case of hepatic liver reported by Allen:[26] A white man 53 years old was struck by a sledge hammer thrown from a passing train. At operation the abdomen was full of blood, and there was a rupture 3 inches (7.6 cm.) long in the dome of the liver. Autotransfusion was done with the removed citrated blood. The patient was in good condition at the end of the operation but died with complete anuria fifty-six hours later. Although noting that the anuria may have been due to other causes, Allen attributed it to the intravenous administration of blood possibly mixed with bile. In our opinion autopsy would have showed typical changes in the liver and kidneys.

It is quite evident from these few cases that after trauma to the liver, exactly as after operations on the gallbladder, and, as we are coming to believe, after any operation on a person with a damaged liver, there may occur a distinctive syndrome. In life it is characterized by hyperpyrexia, with or without associated uremic symptoms, depending on the duration of the illness. At postmortem examination there are found degenerative changes within the liver, associated with renal changes of the same character if the patient has lived long enough. As Helwig and Orr have pointed out, and as we ourselves have observed, when death follows traumatic necrosis of the liver, the hepatic changes are limited to the traumatized area, whereas in nontraumatic states the degenerative changes are diffuse. In either state the damage to the kidneys is generalized.

If our theory of hepatic necrosis as an important if not the most important consideration in trauma to the liver is correct, our outlook on injuries to the liver must be radically changed. Our view is that of Fairchild,[27] who classified injuries of the abdominal viscera as conditions which demand immediate exploration, on the basis of our inability

26. Allen, A. W.: Internal Abdominal Injuries Without Penetrating Wounds, New England J. Med. **205**:34-38 (July 2) 1931.

27. Fairchild, F. R.: Serious Intra-Abdominal Trauma Without External Evidence of Violence, Surg., Gynec. & Obst. **52**:767-775 (March) 1931.

to say that certain lesions do not exist rather than that they do. If an error must be made, he added, surgical treatment is a procedure in which it entails the least fatal consequences. Eliason and McLaughlin,[28] speaking of penetrating wounds, made the same point. The surgeon has no right merely to hope, they said, that the injury has not caused hemorrhage or perforation. It is true that certain surgeons, Hinton [29] and Willis [30] for instance, have achieved excellent results in treating abdominal injuries conservatively, but we question the wisdom of a uniform adoption of their plan.

One point which surgeons who advise against conservative treatment would do well to bear in mind is made by Prey and Foster,[31] in a report from the Denver General Hospital. In their series the average operating time in the fatal cases was one hour and ten minutes, only four consuming less than an hour. In the cases in which the patient survived, the average operating time was fifty-five minutes, and in none was the duration over an hour. Evidently speed in operating plays an important part in the results.

We might add at this point that in none of the patients we have observed or studied was brachycardia present. Almost without exception the patients had pulse rates that were more rapid than normal, sometimes considerably more rapid. Krieg [32] and Wangensteen [33] also warned against trusting this sign, and it is evident that the original observation was not correct.

Exploration, we believe, should be undertaken in every case in which injury to the liver is suspected in which the patient is not actually moribund or in which he can be brought out of his shock and rendered fit for exploration. Transfusion is important in view of the enormous loss of blood which the double blood supply of the liver, from the hepatic artery and the portal vein, makes almost inevitable. Mason,[34] in a discussion of subcutaneous injuries of the abdomen before the American Surgical Association in 1933, called attention to the difficulty

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28. Eliason, E. L., and McLaughlin, C. M., Jr.: Surgical Emergencies of Abdomen, M. Clin. North America **18**:63-80 (July) 1934.

29. Hinton, J. W.: Injuries to Viscera: Their Relative Frequency and Their Management, Ann. Surg. **90**:351-356 (Sept.) 1929.

30. Willis, B. C.: Shotgun Wounds of the Abdomen, Am. J. Surg. **28**:407-427 (May) 1935.

31. Prey, D., and Foster, J. M.: Gunshot Wounds of the Abdomen, Ann. Surg. **99**:265-270 (Feb.) 1934.

32. Krieg, E. G.: Hepatic Trauma, Arch. Surg. **32**:907-914 (May) 1936.

33. Wangensteen, O. H.: Abdominal Injuries, Internat. Surg. Digest **21**:323-335 (June) 1936.

34. Mason, J. M., in discussion on Lewis, D., and Trimble, I. R.: Subcutaneous Injuries of the Abdomen, Tr. Am. S. A. **51**:206-218, 1933.

of securing blood for indigent and friendless Negro patients and stressed the necessity of adopting some systematic measures for emergency transfusion. We echo his ideas, for the problem is one which we meet constantly at the Charity Hospital and against which we can fairly charge more than one personal fatality.

After the abdomen is opened, the procedure should depend on the findings. Abrasions and insignificant injuries do better, as this small series proves, if they are left untouched; suture or packing would simply introduce unnecessary trauma. An extensive laceration or deep wound should be sutured, if that is possible—suture of the liver, as Robertson notes, must be classed among the finer arts—otherwise the wound should be packed. Dragstedt and others have pointed out the damage which can be wrought by packs, their idea being that the pathologic change is obstructive. While this is undoubtedly true, we would emphasize the element of further trauma to the hepatic tissue which can be achieved by tight packing and the possible risk of hemorrhage when the pack is removed. We would also warn against the assumption that simply because a blood clot covers the wound no further bleeding is likely to occur. Unless the depth and character of the wound are known, this is a doubtful assumption, as is proved by the number of secondary hemorrhages noted in our small series of cases and in those reported in the literature. Even a slight rise in blood pressure as the patient comes out of shock may cause such a result.

In cases of extensive wounds in which there is extensive necrosis of the hepatic tissue, we take the position, we believe for the first time, that resection of the involved area best serves the patient's interests. We are quite aware of the risk of cutting into the liver, but we are equally aware, through our experimental and clinical studies, of the dangers of hepatic necrosis. Resection of the liver will always be a serious operation, never to be resorted to lightly and without due thought. But it is a perfectly feasible operation in view of the regenerative properties of this organ. Control of hemorrhage will always be difficult, but methods have been devised by which it can be achieved.

Tinker's [35] report before the American Surgical Association in 1935 brought together, as it were, the possibilities of resection of the liver, and he emphasized, as we do, that when the necessity exists, the operation can be done. We are merely extending his indications. In a paper of our own on primary carcinoma of the liver [36] we cited reports of

35. Tinker, M. B.: Liver Resection: Case Report and Advantages of Radiocutting, Tr. Am. S. A. **53**:247-260, 1935.

36. Boyce, F. F., and McFetridge, E. M.: Primary Carcinoma of Liver, with a Report of Twenty-Eight Additional Cases, Internat. Surg. Digest **18**:67-80 (Aug.) 1934.

several such cases collected from the literature. Yeomans, for instance, performed a second operation for recurrence of this condition seven years after the original growth had been removed. Jackson did a resection of one of the lobes of the liver in a white woman 80 years old who was alive and well seventeen months later. Tinker quoted the experimental work of Fishback, at the Mayo Clinic, which shows that complete regeneration of the liver occurs within six to eight months after four fifths of it has been removed.

The operation, then, is entirely possible. As to the justification, we believe that the case reported by Fabricius Hildanus in the early part of the seventeenth century proves our point. A young man was stabbed in the abdomen and had a severe hemorrhage, which did not prove fatal. Some days later a large piece of liver appeared in the abdominal wound and was removed by forceps. *In spite of this fact,* said Shedden and Johnston,[37] who cited the case, he recovered. *Because of this fact,* we say, his life was saved. By autosurgery, as it were, the products of liver autolysis, which otherwise would probably have killed him, were eliminated from his body.

SUMMARY

We have reviewed previous experimental work on tissue autolysis and have added to it duplicated and original experiments of our own.

From our own experiments and the experiments of others we have concluded that in such cases the products of the autolysis are responsible for the fatal outcome and that the rôle of the gas bacillus is secondary and catalytic. We have pointed out also the effect of the size and condition of the experimental animal and the amount and form of the implanted liver, as well as the effect of autoclaving and incubating the tissue before implantation.

We have pointed out the clinical application of tissue autolysis in such pathologic states as gangrene of the appendix, strangulation obstruction and trauma to tissue.

We have applied our work on tissue autolysis specifically to trauma to the liver and have pointed out the important part which the destruction of hepatic tissue may play in the final result. In this connection we have collected reports of four cases from the literature, in two of which the diagnosis was proved by autopsy, and have added seven of our own, in two of which the diagnosis was proved by autopsy.

We have proposed, in the light of our theory of the danger of tissue autolysis, that exploration be done in all cases in which trauma to the liver is suspected and that resection be undertaken if the necrosis of the hepatic tissue is extensive.

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37. Shedden, W. M., and Johnston, F.: Traumatic Rupture of the Liver, New England J. Med. **213**:960-964 (Nov. 14) 1935.

ACUTE PHLEGMONOUS ENTERITIS

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MacCallum [1] in 1906 reported a case of acute phlegmonous inflammation of the small intestine and reviewed reports of seven similar cases from the European literature. Since his article, the report of one other case has appeared in the American literature (Jones [2]), and it has been possible for us to collect and analyze reports of thirty-two additional cases of this disease that have been described in the foreign literature.

Two examples of this condition were recently seen at necropsy at the Bellevue Hospital. They are presented below, and the previously reported cases are reviewed.

REPORT OF CASES

CASE 1.[3]—J. M., a 46 year old white man, was admitted to the third medical division of the Bellevue Hospital on June 12, 1935. He was a vagrant and suffered from chronic alcoholism; his history was contradictory and unreliable. It was ascertained, however, that about twenty-four hours before his admission to the hospital he had become acutely ill with cramplike pains in the upper part of the abdomen, vomiting, chills and diarrhea. On physical examination he was retching and vomiting. There was diffuse tenderness, more marked on the left side of the abdomen, but there was absence of rigidity. The temperature was 103.2 F., the pulse rate 104, the blood pressure 164 systolic and 94 diastolic (in millimeters of mercury) and the white blood cell count 18,500, with 46 per cent polymorphonuclear leukocytes, 44 per cent metamyelocytes II and 5 per cent lymphocytes.

The following day the patient was delirious and tremulous. His abdomen was resistant, the rigidity being more marked on the left side. There was an ill defined mass, about the size of an orange, in the left lower abdominal quadrant. During the subsequent four days he remained acutely ill, although the vomiting and diarrhea ceased. The temperature fluctuated between 103 and 105 F. A soft mass became palpable in the left upper quadrant and to the left of the umbilicus, which was interpreted as the spleen by some observers. Two blood cultures proved sterile. Death occurred on June 17.

From the Department of Pathology and the Third (New York University) Surgical Division of the Bellevue Hospital and the Department of Pathology of the New York University College of Medicine.

1. MacCallum, W. G.: Phlegmonous Enteritis, Bull. Johns Hopkins Hosp. **17**:254-258, 1906.
2. Jones, E. M.: Phlegmonous Enteritis, Minnesota Med. **14**:956-959, 1931.
3. Dr. John Wyckoff supplied the clinical record of this case.

Significant Necropsy Observations.—Necropsy, performed five days after death, revealed absence of free fluid in the peritoneal cavity. The parietal peritoneum over the anterior wall in the left upper quadrant appeared rough and injected. The first portion of the jejunum was distended. About 50 cm. from the pylorus, and extending distally for 20 cm. without any sharp line of demarcation, the intestine had the character of a rigid, thickened tube. The serosa was deep red and presented several yellowish areas, from 2 to 10 mm. in diameter, from which purulent material could be expressed. A fibrinopurulent exudate was deposited on this portion of the intestine, as well as between coils of intestine in the lower part of the abdomen. The mesentery contiguous with the involved intestine was similarly indurated and presented small foci of suppuration. On section, the affected region of the jejunum showed marked thickening of the submucosal coat. The transverse plicae appeared as markedly swollen and rigid folds without visible evidence of ulceration. The submucosa varied from 5 to 10 mm. in thickness and was uniformly gray (figs. 1 and 2).

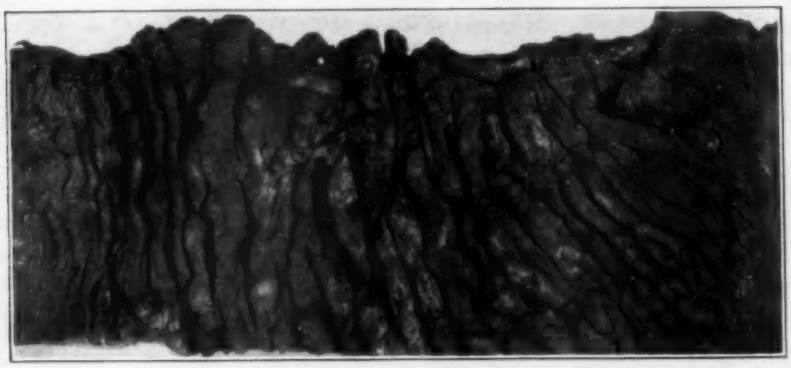

Fig. 1 (case 1).—View of the opened jejunum. Note the markedly swollen plicae circulares, the absence of ulceration of the mucous membrane and the transition from the involved to the uninvolved portions of the intestine. A block has been removed for microscopic study.

Microscopic examination of the involved portion of the jejunum revealed marked diffuse edema, fibrinous exudation and dense polymorphonuclear leukocytic infiltration of the submucosa. The mucous membrane formed a continuous lining, although it appeared to be necrotic or autolyzed. There was a focal extension of the exudate into the muscularis and serosa, where miliary abscesses were encountered. The mesentery presented similar evidence of acute suppurative inflammation. Micro-organisms could not be demonstrated in sections stained by the Gram-Weigert technic or with methylene blue.

The appendix showed atrophic and sclerotic changes. In the lungs were found small tuberculous foci in both apexes and a few scattered minute tubercles in the lower lobes, but neither cavitation nor caseation was present. There was also a small hemorrhagic pulmonary infarct in the upper lobe of the left lung. The other organs exhibited nothing of note.

Summary.—A 46 year old man, with a history of chronic alcoholism, became acutely ill with cramplike abdominal pain, vomiting and diarrhea, chills, fever

and leukocytosis. Abdominal examination revealed tenderness and inconstant rigidity of the left side of the abdomen, accompanied by an ill defined mass in the left upper quadrant and to the left of the umbilicus. Death occurred six days after the onset of symptoms. Necropsy revealed an acute diffuse fibrinopurulent inflammation of 20 cm. of the jejunum, affecting chiefly the submucosal coat, without mucosal ulceration, and extending to the serosa and into the mesentery. A localized fibrinopurulent peritonitis accompanied this extension.

Case 2.—J. P., a 45 year old white man, was admitted to the psychiatric service of the Bellevue Hospital on April 10, 1936. He was confused and disoriented, and efforts to obtain a coherent history were unsuccessful. He appeared chronically ill but was not in acute distress. The abdomen showed distention and tympany, spasticity, which was more marked on the right side, and tenderness of the right lower quadrant. The temperature was 98 F., the pulse rate 110, the blood pressure 114 systolic and 74 diastolic and the white blood count 12,500, with 71 per cent polymorphonuclear leukocytes, 14 per cent metamyelocytes II and 15 per cent lymphocytes.

In the following forty-eight hours the patient lapsed into a semicomatose state, and bladder and rectal incontinence developed. No vomiting was observed,

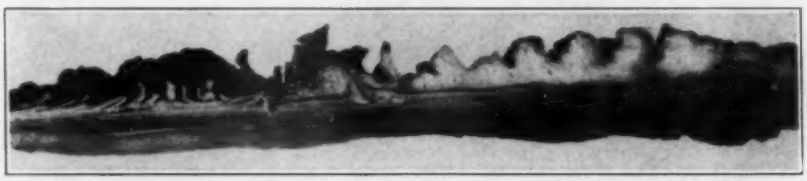

Fig. 2 (case 1).—A side view of the wall of the opened jejunum, showing the marked swelling of the plicae circulares.

but numerous watery stools were passed. The abdominal signs did not change. The temperature varied between 98 and 101 F., the blood pressure dropped to 80 systolic and 60 diastolic, the urine showed a trace of albumin and the nonprotein nitrogen content of the blood was 100 mg. per hundred cubic centimeters. Death occurred forty-eight hours after admission.

Significant Necropsy Observations.—Necropsy, performed six days after death, showed 500 cc. of a yellow slightly sanguineous fluid with flakes of fibrin in the peritoneal cavity. The peritoneum was dull and lusterless. There were many fresh fibrinous adhesions between loops of the small intestine. There was marked distention of the upper loops of the small intestine, diminishing gradually in the ileum. Near the termination of the ileum, for a distance of about 30 cm., the intestine was heavy and firm and appeared gray, with a thick fibrinous deposit on the serosa. On section, the distal portion of the ileum presented a thickened, firm, gray appearance, with prominent circular plicae and a soft gray submucous coat about 5 mm. in thickness. There was no apparent ulceration of the mucosa and no evidence of hemorrhage or gangrene. The process began gradually about 50 cm. above the ileocecal valve and ended abruptly about 20 cm. above the latter. The adjacent mesentery was indurated and exhibited purulent foci. The branches of the mesenteric artery at the attachment of the intestine were plugged by soft grayish red thrombotic masses, which extended proximally up to the point of bifurcation of a branch of the second order. The latter, as well as the larger

branches and the trunk of the superior mesenteric artery, exhibited a smooth intima. The mesenteric and portal veins were natural.

Microscopic examination of the involved section of ileum revealed marked thickening of the wall due, chiefly, to edema, fibrinous exudation and dense infiltration by polymorphonuclear leukocytes in the submucosal layer (fig. 3). The mucous membrane, although exhibiting focal acute inflammatory and necrotic changes, was not ulcerated. The muscular layers presented well preserved muscle bundles, between which were many polymorphonuclear leukocytes. The serosa in some sections appeared intact and in others showed a dense exudate of polymorphonuclear leukocytes and fibrin. Bacilli and cocci, the latter in short chains and diplococcus forms, were demonstrated on the mucous membrane and in the submucosa by the Gram-Weigert technic.

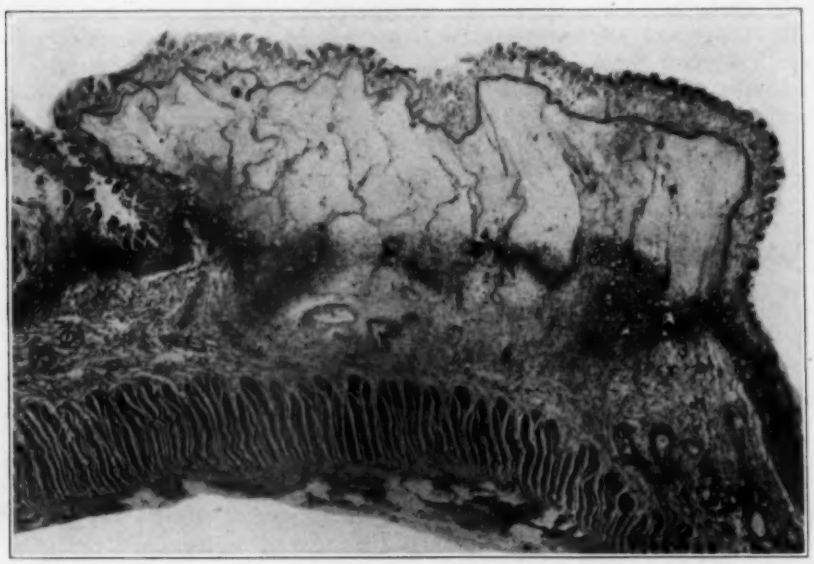

Fig. 3 (case 2).—View of a section of the ileum showing the marked thickening of the submucosal coat with edema, fibrin formation and infiltration by polymorphonuclear leukocytes. The mucous membrane forms a continuous lining. Hematoxylin and eosin stain.

There was dense infiltration of the mesentery by polymorphonuclear leukocytes, and the mesenteric lymph nodes presented evidence of acute inflammation.

Some of the small arteries in the tunica propria and submucosa showed infiltration of their walls by polymorphonuclear leukocytes and were plugged by homogeneous eosinophilic masses. The thrombosed branches of the superior mesenteric artery appeared in sections to be filled by recent thrombi composed largely of red cells and fibrin. There were no inflammatory or arteriosclerotic changes in these vessels, although there was a diffuse suppurative inflammation of the mesentery through which these vessels coursed. A few small venous channels were also plugged by recent thrombi. In one of the sections through the mesentery an artery was found, about 1 mm. in diameter, containing an organized and canalized thrombus.

In the appendix were found atrophy of the lymphoid elements and a diffuse increase in the fibrous tissue of the submucosa. Plasma cells and eosinophilic polymorphonuclear leukocytes were present in moderate number throughout the mucous membrane.

The liver presented fatty change, and there were congestion and edema of the lungs.

Summary.—A 45 year old white man, from whom a coherent history was not obtainable, died forty-eight hours after admission to the hospital with the clinical picture of mental confusion and disorientation, abdominal distention, spasticity and tenderness of the right lower abdominal quadrant, leukocytosis and shock. Necropsy revealed acute diffuse fibrinopurulent inflammation of about 30 cm. of ileum, affecting chiefly the submucosal coat and extending to the serosa and into the mesentery. The mucous membrane was not ulcerated. There was terminal thrombosis of some of the branches of the mesenteric vessels in the involved intestine and mesentery; in one section through the mesentery a small artery was found containing a completely organized and canalized thrombus.

REVIEW OF THE LITERATURE

Acute phlegmonous enteritis was mentioned by Rokitansky [4] in 1842 and called "enteritis submucosa suppurativa." Bohmansson,[5] who summarized the literature in 1923, accepted as cases of acute phlegmonous enteritis those in which an "acute, purulent inflammatory process in the submucosa and subserosa of the intestine" was reported. The cases recorded in the literature as instances of "phlegmonous enteritis" or *Darmphlegmone*, and which we have selected for the review of the pathologic and clinical features of this disease, represent instances of an apparently primary suppurative lesion of the intestinal wall, affecting chiefly the submucosal coat. Localized suppurative lesions of the intestine secondary to ulcer or carcinoma are not considered. The relationship of this lesion to a similar or identical process in the stomach and large intestine and to regional subacute and chronic nonspecific inflammatory lesions of the intestine will be considered.

Distribution of the Lesion.—Of forty-one reported cases, the lesion in twelve was localized to the duodenum or the duodenum and the proximal portions of the jejunum,[6] in twenty-two the jejunum alone was involved [7] and in seven the lesion was limited to the ileum.[8]

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4. Rokitansky, C.: Lehrbuch der pathologischen Anatomie, Vienna, Wilhelm Braümuller, 1842.

5. Bohmansson, G.: Acute Purulent Processes in the Intestinal Wall, Acta chir. Scandinav. **55**:437-489, 1922-1923.

6. (*a*) Askanazy, M.: Ueber Enteritis phlegmonosa, Centralbl. f. allg. Path. u. path. Anat. **6**:313-319, 1895. (*b*) Deutelmoser, cited by MacCallum.[1] (*c*) Ungermann, E.: Duodenitis phlegmonosa, Virchows Arch. f. path. Anat. **193**: 445-455, 1908. (*d*) Neupert: Demonstration eines Präparates von Enteritis phlegmonosa, Zentralbl. f. Chir. **37**:713, 1910. (*e*) Taylor, G., and Lakin, C.: A Fatal Case of Phlegmonous Inflammation of the Duodenum Fol-

(Footnotes continued on next page)

Age and Sex.—The distribution of patients in the various decades is as follows: first decade, one; second decade, none; third decade, three; fourth decade, seven; fifth decade, four; sixth decade, twelve; seventh decade, nine; eighth decade, two; ninth decade, one. Thirty of the cases were in males and nine in females. In two cases the age and sex of the patient were not given.

Etiology and Pathogenesis.—The bacteriologic picture as well as the histopathologic features suggest that the lesion is due to invasion of the wall of the intestine by pyogenic micro-organisms. In a few instances cultures have been made of the pus in the intestinal wall. The micro-organisms obtained have been "Streptococcus," [9] Staphylococcus,[5] Pneumococcus,[7h] Bacillus coli [6e] and Staphylococcus and "Streptococcus" together.[6a] More commonly, micro-organisms have been demonstrated in sections of the tissue or in direct smears of the pus, and in most instances the presence of "streptococci" or gram-positive cocci in short chains or diplococcus forms is recorded.[10] In a few instances the presence of micro-organisms could not be verified in sections.[11]

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lowing Impaction of a Fish Bone, Lancet **2**:224-225, 1911. (*f*) Black, K.: Two Cases of Phlegmonous Duodenitis, Practitioner **95**:104-107, 1915. (*g*) Frising, G., and Sjövall, E.: Die phlegmonose Enteritis in Duodenum und Anfangsteil des Jejunums, Beitr. z. klin. Chir. **83**:1-25, 1913. (*h*) Hellström, N.: Zur Kenntnis der primären Phlegmone im Darm, ibid. **115**:602-628, 1919. Bohmansson.[5]

7. (*a*) Bellfrage and Hedenius. (*b*) Moissejew; Hoffman, and Neupert, cited by MacCallum.[1] (*c*) Müller, W.: Ein Beitrag zur Pathologie der Dünndarmphlegmonen, Virchows Arch. f. path. Anat. **216**:416-423, 1914. (*d*) von Saar, G. F.: Zur Kenntnis der phlegmonösen Prozesse des Darmkanals, Arch. f. klin. Chir. **106**:228-234, 1915. (*e*) Holmdahl, D. E.: Beitrag zur Kenntnis der eitrigen, ulcerösen, und diphtheritischen Prozesse im Dünndarm, Beitr. z. klin. Chir. **99**: 193-227, 1916. (*f*) Zoepffel, H.: Heilung der Enteritis phlegmonosa durch Darmresektion, Deutsche Ztschr. f. Chir. **154**:266-270, 1920. (*g*) Wilson, J. B. F.: Acute Primary Phlegmonous Enteritis, Lancet **1**:1244, 1922. (*h*) Leuchtenberger, R.: Zur Kasuistik der Darmphlegmone, Virchows Arch. f. path. Anat. **246**:418-425, 1923. (*i*) Bundschuh, E., and Wolff, E. P.: Zur Kenntnis der Darmphlegmone, Arch. f. klin. Chir. **136**:438-448, 1925. (*j*) Krüger, H.: Ueber Ileus durch Dünndarmphlegmone, ibid. **153**:813-815, 1928. (*k*) Irwin, C. G., and McDonald, S.: Two Cases of Localized Phlegmonous Enteritis, Brit. J. Surg. **19**:362-373, 1932. MacCallum.[1] Bohmansson.[5] Neupert.[6d] Hellström.[6h]

8. (*a*) Glaus, A.: Ueber primäre Enteritis phlegmonosa staphylococcica ilei, Berl. klin. Wchnschr. **55**:474-477, 1918. (*b*) Fromme: Berichte aus den Chirurgischen Gesellschaften, Zentralbl. f. Chir. **51**:2386, 1924. (*c*) Metge, E.: Beitrag zur Kenntnis der primären Darmphlegmone, ibid. **52**:2474-2475, 1925. (*d*) Neugebauer, F.: Phlegmone des Ileums, Beitr. z. klin. Chir. **144**:228-230, 1928. (*e*) Nash, F. W. B.: Acute Localized Phlegmonous Enteritis Complicating Pregnancy, Brit. M. J. **2**:792-793, 1932. Jones.[2] Bohmansson.[5]

9. Hellström.[6h] Bundschuh and Wolff.[7i]

10. MacCallum.[1] Bohmansson.[5] Ungermann.[6c] Neupert.[6d] Frising and Sjövall.[6g] Hellström.[6h] Moissejew, cited by MacCallum.[1] Müller.[7c] Irwin and McDonald.[7k] Neugebauer.[8d]

11. Hellström.[6h] Zoepffel.[7f]

Although the infection is frequently assumed to be of enterogenous origin, few reports offer a convincing demonstration of the portal of entry. Changes in the mucous membrane are not constantly present, and the character of the mucous membrane lesion suggests that it is secondary to the process in the submucosa. Various suggestions have been presented concerning the influence responsible for the penetration of organisms from the lumen into the wall of the intestine. In the case reported by Askanazy [6a] the onset of symptoms was preceded several days before by abdominal trauma, which was interpreted as the inciting cause, although no visible defect was demonstrated in the mucous membrane of the involved jejunum. In MacCallum's [1] case, too, abdominal trauma occurred several days preceding the onset of symptoms. In a case reported by Ungermann [6c] duodenal diverticuli containing sharp bony spicules were found in the phlegmonous lesion, and in another case (Taylor and Lakin [6e]) impaction of a fish bone was demonstrated in the wall of the involved duodenum. Part of a fish bone was found in the duodenal contents in a case reported by Frising and Sjövall.[6g] Intestinal parasites (Oxyuris) have been reported in one instance (Fromme [8b]). In four cases the phlegmonous intestinal lesion complicated atrophic cirrhosis of the liver,[12] and Leuchtenberger [7h] suggested that "intestinal catarrh" due to portal stasis may play a predisposing rôle. In two instances the disease complicated pregnancy.[13]

There is no convincing evidence that the infection is ever of hematogenous nature. The lesion has occurred as a complication of pneumococcic pneumonia in two instances,[14] of scarlet fever in one instance [2] and of acute tonsillitis in another; [5] but an enterogenous source of pyogenic organisms cannot be excluded in these instances.

Further support for the belief in the enterogenous nature of the infection is to be gained by consideration of the comparative frequency of the phlegmonous lesion in different parts of the gastro-intestinal tract. In the stomach as well as in the colon there occurs an acute phlegmonous lesion which is closely similar in its histopathologic and bacteriologic features and clinical course to the acute phlegmonous lesion of the small intestine. However, acute phlegmonous gastritis apparently occurs much more frequently than the analogous lesion in the intestine. Szabó [15] in 1934 stated that there were two hundred and fifty-three cases of gastric phlegmon reported in the literature. Acute

12. Matthes, cited by MacCallum.[1] Neupert.[6d] Leuchtenberger.[7h] Bundschuh and Wolff.[7i]

13. Bohmansson.[8] Neugebauer.[8d]

14. Wilson.[7g] Leuchtenberger.[7h]

15. Szabó, K.: Einiges über Magen und Darmphlegmonen, mit Rücksicht auf zwei Dickdarmphlegmonenfälle, Zentralbl. f. Chir. **61**:947-952, 1934.

phlegmon of the colon occurs much less commonly. Of thirteen proved cases reported in the literature, the lesion in six was limited to the cecum,[16] in four to the cecum and ascending colon,[17] in one to the transverse colon,[18] in one to the descending colon[19] and in one to the sigmoid colon.[6h]

The greater predilection of the lesion for the stomach and the upper portion of the small intestine and the diminishing incidence of the lesion in the distal portion of the gastro-intestinal canal suggest that the causative organisms are swallowed. It has been emphasized that chronic gastritis is a frequent finding in acute phlegmonous gastritis, and it has been suggested that the former lesion predisposes to the latter by lowering or abolishing the acidity and bactericidal power of the gastric juice.[20] The high incidence of chronic alcoholism in phlegmonous gastritis is interpreted as further evidence of the rôle of chronic gastritis and anacidity in the genesis of the phlegmonous lesion (Konjetzny and Schnarrwyler[21]).

A similar correlation in phlegmonous lesions of the intestine has not yet been established, although the rôle of chronic gastritis has been suggested.[22] Hellström[6h] called attention to the history of chronic alcoholism in two of Müller's cases, it was noted by Bsteh[16a] in an instance of phlegmonous cecitis, and it was present in case 1 of this report.

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16. (*a*) Bsteh, O.: Zur Kenntnis der Darmphlegmone, Arch. f. klin. Chir. **169**:193-203, 1932. (*b*) Teutschlaender, O., and Valentin, B.: Enteritis phlegmonosa (durch Darmresektion geheilte Caecumphlegmone), Mitt. a. d. Grenzgeb. d. Med. u. Chir. **38**:469-480, 1924-1925. (*c*) Pataky, Z.: Mit Dickdarmphlegmone komplizierter Appendicitisfall, Zentralbl. f. Chir. **54**:1566-1568, 1927. (*d*) Köntzey, E., and Jáki, J.: Ueber einen Fall von primärer Coecumphlegmone, ibid. **55**: 1223-1226, 1928. (*e*) Bundschuh and Wolff.[7l]

17. Biederman, H.: Durch Darmresektion geheilte primäre Phlegmone des Dickdarms mit Inversion der Coecalwand, Beitr. z. klin. Chir. **124**:718-721, 1926. (*b*) Ingier, A.: Ein Fall von Pneumokokkenmetastase im Colon ascendens, Centralbl. f. allg. Path. u. path. Anat. **21**:148-156, 1910. (*c*) von Saar.[7d] (*d*) Leuchtenberger.[7h]

18. Goldschmidt, F.: Ein Fall von Enteritis phlegmonosa, Arch. f. klin. Med. **40**:400-404, 1887.

19. Dowd, C. N.: Acute Phlegmonous Inflammation of the Large Intestine, Ann. Surg. **56**:579-581, 1912.

20. Konjetzny, G. E.: Gastritis phlegmonosa, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928, vol. 4, pt. 2.

21. Schnarrwyler, cited by Adams, J. E.: Acute Primary Phlegmonous Gastritis, Lancet **1**:292-296, 1910.

22. Frising and Sjövall.[6g] Hellström.[6h]

Pathologic Picture.—Localized fibrinous peritonitis is usually present, and in the majority of instances a turbid effusion or a generalized purulent peritonitis is also found. Occasionally a serous effusion occurs.[23] Peritonitis occurs without demonstrable perforation of the intestine and may be present within twenty-four hours of onset [6h] or absent as late as the fifth day of the disease.[7d]

The phlegmonous lesion involves the intestine in a uniform diffuse manner for a variable distance.[24] Usually from 15 to 40 cm. of intestine is affected by the phlegmonous lesion, though the latter may be as limited as 4 cm.[7e] or as extensive as 60 cm.[7f] There is no apparent correlation between the duration of symptoms in different subjects and the length of the phlegmon. Except in the case described by Matthes,[25] in which the phlegmonous lesion involved the entire gastro-intestinal canal, coexistence of a gastric and intestinal phlegmon or of the latter and a phlegmon of the colon has not been described. The involved portion of the intestine is sometimes sharply demarcated from the uninvolved area, or the division may be more gradual. Proximal or distal to the phlegmon, the intestine may exhibit extensive edema.

The more characteristic features of the involved intestine are its stoutness, its heaviness and its rigidity. It may be swollen to from three to four times its normal diameter and feels indurated and inflexible. The serosa is frequently red and edematous and possesses fibrinous deposits or yellowish gray purulent foci. After the intestine is opened, the swollen and rigid character of the plicae circulares proves striking; these circular folds may measure a centimeter or more in thickness. On the cut surface of the intestinal wall may be seen the broadly thickened translucent gray submucosa. The thickening of the submucosa, and particularly of the transverse plicae, may produce stenosis of the lumen of the viscus. The mucous membrane in most instances appears gray and edematous but is otherwise intact; less often there is focal necrosis, suppuration or ulceration. Small scattered abscesses are frequently found in the submucosa and extend into the lumen or subserosa.

The contiguous mesentery is frequently edematous and sometimes involved in the phlegmonous process. In duodenal phlegmon there may be edema and infiltration, by polymorphonuclear leukocytes, of the retroduodenal tissue and the pancreas.[6g] The mesenteric lymph nodes are enlarged and occasionally suppurative. Large abscesses of the mesentery accompanying acute phlegmonous enteritis have been noted by Müller [7c]

23. Black.[6f] Zoepffel.[7f]

24. Instances of localized abscesses or inflammatory nodules in the intestinal wall are described by Bsteh [16a] and Bohmansson.[5]

25. Matthes, cited by MacCallum.[1]

and Bohmansson.[5] Thrombosis of the regional arteries or veins, as observed in case 2, has not been recorded in the reported cases.

The microscopic picture is that of edema, fibrinous inflammation and dense diffuse infiltration by neutrophilic polymorphonuclear leukocytes, the process affecting chiefly the submucosa. The mucous membrane may appear normal or show edema, acute inflammation or necrosis. In the case reported by Metge[8c] the inflammatory cells were chiefly eosinophilic polymorphonuclear leukocytes.

Symptoms and Signs.—In most instances the disease is characterized by the sudden onset of intense abdominal pain, which is epigastric or periumbilical in nature. Frequently the pain is colicky. Vomiting constantly follows and may become fecal. Often a chill occurs early in the disease.[26] Obstipation is commonly observed, although diarrhea occasionally occurrs. Blood may rarely appear in the stool.[7f] Jaundice occurred in a few instances in which the first part of the duodenum was involved.[27]

The patient generally appears acutely and critically ill. The abdomen is frequently distended, and tenderness is present in the epigastrium, periumbilical region or right lower quadrant. Rigidity is absent as frequently as it is present. In a few instances, as in case 1, an ill defined mass may be palpated.

Fever and leukocytosis are present in most cases, the former ranging from 100 to 104 F. However, the temperature is not infrequently normal.[28]

Prognosis and Treatment.—In the cases analyzed in this report thirty-four of the patients died within from thirty hours to a week after the onset of symptoms. In one case the course was more prolonged, death occurring on the fortieth day.[6b] In no instance has a correct preoperative diagnosis been made; the patients have come to operation most frequently with the diagnosis of acute appendicitis or intestinal obstruction. Twenty-two died without surgical intervention. Laparotomy was done in thirteen cases in which death occurred, resection being performed in three and enterostomy, gastro-enterostomy or drainage in ten.

In seven cases recovery occurred after resection of the involved intestine. Of the cases in which recovery followed resection, in five the condition was acute phlegmonous ileitis,[29] and in two, acute phleg-

26. Black.[6f] Frising and Sjövall.[6g] Hellström.[6h] Bellfrage and Hedenius.[7a] Irwin and McDonald.[7k]

27. Deutelmoser, cited by MacCallum.[1] Ungermann.[6e] Frising and Sjövall.[6g] Holmdahl.[7e]

28. Frising and Sjövall.[6g] Zoepffel.[7f] Krüger.[7j]

29. Bohnmansson.[5] Fromme.[8b] Metge.[8c] Neugebauer.[8d] Nash.[8e]

monous jejunitis.[30] The length of the involved intestine in these cases varied from 8 to 50 cm. It is noteworthy that in the seven instances in which the involvement was limited to the ileum, five of the patients recovered, whereas only two of the twenty-three patients with acute phlegmonous jejunitis recovered. This is at least partly due to the difficulties of performing a resection when the proximal portion of the jejunum is involved. In this connection it is to be noted that six of thirteen patients with acute phlegmonous colitis recovered after resection of the involved intestine.[31]

Whether recovery can occur without resection is impossible to affirm, for in the absence of a resected specimen a convincing diagnosis is not possible. Several reports exist in which the findings at operation suggested the presence of a phlegmon of the intestine, and recovery occurred without resection.[32] Most convincing is the case described by Wilson,[7g] in which recovery followed a lateral anastomosis above and below the affected portion of the jejunum.

Relationship of Acute Phlegmonous Enteritis to Chronic Nonspecific Inflammatory Lesions of the Intestines.—Recently, many reports have appeared of chronic nonspecific inflammatory lesions involving the small or large intestine, to which various designations have been assigned, namely: inflammatory tumor,[33] chronic interstitial enteritis,[34] nonspecific granuloma of the intestine,[35] regional ileitis,[36] nonspecific granuloma of the gastro-intestinal tract,[37] chronic cicatrizing enteritis [38] and regional enteritis.[39]

The etiology of this lesion in most cases is obscure. It is possible that in some instances an acute localized phlegmonous process due to pyogenic cocci may form a chronic nonspecific productive inflammatory

30. Bohmansson.[5] Krüger.[7j]

31. von Saar.[7d] Brundschuh and Wolff.[7l] Teutschlaender and Valentin.[16b] Pataky.[16c] Biederman.[17a] Dowd.[19]

32. Jones.[2] Bohmansson.[5]

33. Braun, H.: Ueber entzündliche Geschwülste am Darm, Deutsche Ztschr. f. Chir. **100**:1-12, 1909.

34. Dalziel, T. K.: Chronic Interstitial Enteritis, Brit. M. J. **2**:1068-1069, 1913.

35. Moschcowitz, E., and Wilensky, A. O.: Nonspecific Granulomata of Intestine, Am. J. M. Sc. **166**:48-66, 1923.

36. (*a*) Crohn, B. B.; Ginzburg, L., and Oppenheimer, G. D.: Regional Ileitis, J. A. M. A. **99**:1323-1329 (Oct. 15) 1932. (*b*) Koster, H.; Kasman, L. P., and Sheinfeld, W.: Regional Ileitis, Arch. Surg. **32**:789-809 (May) 1936.

37. Erdmann, J. F., and Burt, C. V.: Nonspecific Granuloma of Gastro-Intestinal Tract, Surg., Gynec. & Obst. **57**:71-80, 1933.

38. Donchess, J. C., and Warren, S.: Chronic Cicatrizing Enteritis with Involvement of Cecum and Colon, Arch. Path. **18**:22-29 (July) 1934.

39. Brown, P. W.; Bargen, J. A., and Weber, H. M.: Regional Enteritis, Proc. Staff Meet., Mayo Clin. **9**:331, 1934. Meyer, K. A., and Rosi, P. A.: Regional Enteritis (Non-Specific), Surg., Gynec. & Obst. **62**:977-988, 1936.

lesion. In the literature many cases of a similar chronic intestinal lesion are recorded under the term *Darmphlegmone*,[40] and several authors have presented cases which were interpreted as representing transitional stages between an acute and a subacute or chronic phlegmonous process due to pyogenic cocci.[41] In the stomach, too, lesions have been observed which suggested that acute phlegmonous gastritis caused by pyogenic cocci may pass into a subacute or chronic stage (Konjetzny [20]).

The following case, observed at Bellevue Hospital, illustrates one in which the lesion may represent a transitional stage between the acute phlegmonous and the chronic nonspecific regional type.

CASE 3.—J. K., a 34 year old woman, was admitted to the third surgical division of the Bellevue Hospital in September 1923. Pain in the right lower abdominal quadrant appeared a week before her admission and was followed by nausea and feverishness. Abdominal examination revealed moderate rigidity and marked tenderness in the right lower quadrant. The temperature was 100.5 F.; the white blood count was 8,900 with 91 per cent neutrophilic polymorphonuclear leukocytes.

At operation, performed the day of the patient's admission, the terminal 21 cm. of ileum and cecum was found to be thickened and rigid. The appendix appeared to be normal. The involved portion of the ileum and the cecum were resected, and a lateral anastomosis performed. After two weeks of slight purulent discharge, the wound closed, and the patient made an apparent recovery.

She remained free from symptoms, until August 1929, at which time she reentered the hospital because of abdominal discomfort and fever. She was febrile for about four weeks, during which time she received several transfusions of blood, and gradually the abdominal pain and fever subsided. A similar episode occurred again in February 1930. In August 1932 she again entered the hospital with an abscess of the lower anterior abdominal wall. After incision and drainage of the abscess, multiple fecal fistulas appeared. Ileosigmoidostomy was performed in January 1933, but the fistulas have not yet entirely closed.

The resected specimen presented for examination about 20 cm. of the lower part of the ileum together with the cecum and appendix. The wall of the intestine was thickened, and the mucosa was injected. The mesentery contained a small abscess cavity.

Microscopic sections revealed diffuse thickening of the wall of the intestine, chiefly of the submucosal coat. The mucosa exhibited focal superficial ulceration and dense infiltration by neutrophilic polymorphonuclear leukocytes, lymphocytes and plasma cells. The submucosa, muscularis and serosa showed diffuse infiltration by abundant eosinophilic and neutrophilic polymorphonuclear leukocytes, plasma

40. (*a*) Sauer, H.: Streptokokkenplegmone des Colon ascendens im Anschluss an eine durch Trichocephalus entstandene entzündliche Dickdarmgeschwulst, Deutsche Ztschr. f. Chir. **180**:27-36, 1923. (*b*) Fischer, A.: Ueber Phlegmone der Darmwand, Zentralbl. f. Chir. **58**:1243-1247, 1931. (*c*) Fossel, M.: Ueber einen Fall von operativ geheilter Darmphlegmone, ibid. **59**:1160-1165, 1932. (*d*) Ostrowski, S.: Zur Klinik der Dünndarmphlegmone. Rezidiv 4 Monate nach erfolgreicher Primärresektion, ibid. **60**:501-509, 1933. (*e*) Peters, K. O.: Drei weitere Fälle von Darmphlegmone im Ileum, ibid. **61**:1208-1216, 1934. (*f*) Konjetzny, G. E.: Phlegmone des Dünn- und Dickdarms auf der Grundlage einer einfachen Enteritis bzw. Colitis erosiva, ibid. **62**:978-987, 1935. (*g*) Teutschlaender and Valentin.[16b]

41. Teutschlaender and Valentin.[16b] Sauer.[40a] Ostrowski.[40d] Konjetzny.[40f]

cells, lymphocytes and fibroblasts. In the cecum there was considerable increase in the subserosal tissue, with numerous young histiocytes and fibroblasts. The abscess in the mesentery was filled with polymorphonuclear leukocytes and was surrounded by a wall of granulation tissue.

Although it must be admitted that the anatomic characteristics of certain specimens suggest a close relationship between the acute phlegmonous and the chronic forms, there is no convincing evidence that they are of identical etiology. It is noteworthy that in the small intestine the majority of acute phlegmonous lesions occurred in the duodenum or jejunum (thirty-four of forty-one), whereas the majority of chronic lesions were limited to the terminal portion of the ileum (sixty-five of eighty [36b]). Similarly, reports of chronic regional nonspecific inflammatory lesions of the colon appear in the literature much more frequently than do reports of acute phlegmonous colitis.[36b] Whether this points to a different etiology of the acute phlegmonous and chronic lesions or is a reflection of a variation in the course of the disease in different portions of the gastro-intestinal canal cannot be determined.

SUMMARY

Two fatal cases of acute phlegmonous enteritis are reported, in one the condition being limited to the jejunum and in the other to the ileum.

The pathologic and clinical characteristics in forty-one similar cases reports of which were gathered from the literature are reviewed. It appears that acute phlegmonous enteritis is a well defined clinical and pathologic entity, and although it is most likely an infection of the wall of the intestine with pyogenic micro-organisms of enterogenous origin, a portal of entry is only rarely demonstrated.

The possible relationship of the acute phlegmonous lesion of the intestine to chronic nonspecific inflammatory lesions of the intestine is discussed, and a case is presented which suggests a transitional stage between the two.

SCLEROSING SARCOMA OF BONE

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BALTIMORE

In the older literature, both pathologic and surgical, sarcomas of bone were usually divided into the central and the periosteal type. The central type was frequently referred to as telangiectatic because of its hemorrhagic appearance on macroscopic examination and the absence of any clearly defined picture on microscopic examination. Tumors which are now referred to as osteolytic sarcoma, small round cell sarcoma of bone (Ewing's tumor) and central chondrosarcoma were also considered to be of this type. According to the older classification, periosteal sarcoma likewise had no well defined histologic characteristics. The fibrocellular forms, now recognized as either fascial sarcoma, or sarcoma arising from the nerve sheath and secondarily involving bone, and chondrosarcoma, which in the early stage is mostly subperiosteal and outside of the cortical bone, were classified under the periosteal type. Sclerosing sarcoma, which develops from the periosteum and cortical bone, usually at the ends of the long bones, was also included in this classification.

Bloodgood[1] in 1923 made the following statement concerning the roentgenographic picture in a case referred to him:

> I can also see a somewhat wedge-shaped area occupying the inner head of the tibia, its base towards the periosteal growth in which the normal architecture of the cancellous bone is blurred by a cloudy defect. This means that there is either a periosteal growth of tissue, or an infiltration in the cancellous bone. In my experience this x-ray picture is more often seen in sclerosing sarcoma than in any inflammatory lesion and until recently we never had an opportunity to observe an early picture such as this.
>
> A number of radiologists and surgeons saw this picture, and apparently the opinion of all favored a diagnosis of a low grade of osteomyelitis or tuberculosis. I have before me the typewritten copy of a number of examinations and interpretations of this case. Every examination was negative, except for this change in the x-ray, and the palpation of the soft, tender swelling, as noted above.
>
> The lateral views, made November 1st, show no evidence of periosteal bone formation, but only the slight cloudy defect of the upper end of the tibia.

In a discussion of this case Bloodgood stated:

> My studies agree with Ewing that this is a distinct type, and I propose in a second communication to make a careful study with illustrations of this type of

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From the Laboratory of Surgical Pathology of the Johns Hopkins Hospital.

1. Bloodgood, Joseph Colt: J. Radiol. 4:46 (Feb.) 1923.

sarcoma. . . . My studies so far seem to be convincing that the sclerosing type of sarcoma of bone should be recognized in the x-ray. Its treatment will depend upon the point of view of the one responsible, the choice being between x-ray and radium radiation, and exploration, with further diagnosis by gross and frozen section, followed by resection or amputation.

DIAGNOSIS

The sclerosing sarcoma of bone on microscopic examination is found to be composed of large amounts of osseous and osteoid tissue which originate in the tumor. Such a tumor presents distinctive clinical characteristics. A sarcoma of this type may develop in any of the bones of the skeleton, but it develops relatively rarely in any but the long bones. The series reported here consists of 158 cases. In 4 the tumor developed in the skull, in 10 in the upper and lower jaws, in 3 in the vertebrae, in 4 in the bones of the pelvis and in 4 in the scapula. Not a tumor developed in the bones of the hands or feet. Of the long bones, the femur and the tibia are most frequently affected, and the lower end of the femur and the upper end of the tibia most often are the seat of tumor formation. Seventy-two of these tumors, approximately one half, occurred in the lower end of the femur or the upper end of the tibia.

Sclerosing sarcoma of bone develops most frequently in adolescents and in young adults. In 68 cases the tumor developed in patients who were from 15 to 24 years of age; in 28, in those from 14 to 15. Fourteen of the patients were from 25 to 34 years of age, and but 12 were over 35. Adults are more frequently affected when the tumor develops in the bones of the skull and in the jaws.

The tumor runs a relatively acute course, the duration of symptoms rarely being more than six months. Pain, swelling and impairment of function appear in this sequence. In approximately one half of the cases trauma was mentioned in connection with the beginning of the tumor. Pathologic fracture is rare and occurred in but 7 of the cases being reported. Fever and leukocytosis are less frequently noted than in Ewing's sarcoma. In cases in which fever was reported the temperature did not exceed 101 F., and the leukocyte count was usually under 18,000. These findings, which at times simulate those of osteomyelitis, are observed more frequently in children than in young adults. Nothing of especial significance is revealed by physical examination in the early stage. Cutaneous changes are found only in the advanced stages. Occasionally on palpation crepitus may be made out. It is caused by displacement by pressure of the spicules which radiate from the periosteum. The swelling is usually firm, continuous with the bone and smooth and elliptic.

The final diagnosis is based on the roentgen and the microscopic picture. In the long bones the tumor develops in the end of the bone on the shaft side of the epiphysial line. The most common sites for development are the lower end of the femur and the upper end of the tibia. Some degree of periosteal reaction is usually found, but the earliest evidence of tumor formation is sclerosis, which obliterates the normal markings of the bone in the part involved. The increased density shown by the roentgenogram differs from that found in Ewing's tumor and in Garré's sclerosing osteomyelitis. In the early stages of the sclerosing sarcoma a triangle of bone at one side of the metaphysis is affected, and the most marked involvement of the cancellous bone is found immediately adjacent to the epiphysial line. Rarely does such a tumor extend down the shaft any distance. The earliest indication of tumor formation on the part of the periosteum are spicules of bone laid down at right angles to the shaft. In Ewing's sarcoma the middle of the shaft of the bone is primarily affected as a rule, and the tumor usually extends along the shaft for half of its length. An anteroposterior roentgenogram reveals symmetrical involvement, the periosteum is raised and split longitudinally and radiating spicules of bone are not seen. Osseous destruction is found in the cortical and medullary parts of the bone in the early stages of Ewing's tumor but occurs in the late stages of sclerosing sarcoma. Even in sarcoma in the advanced stage sclerosis is more pronounced than osteolysis.

In Garré's sclerosing osteomyelitis, as in Ewing's tumor, the middle of the shaft is the part usually affected. The bone is symmetrically enlarged by new bone, the cortex becomes widened and the marrow cavity is obscured. This inflammatory lesion of bone may cause an "onion peel" appearance, such as is seen in Ewing's tumor, but the radiating spicules, such as those seen in sclerosing sarcoma, are usually wanting. There is generally no evidence of osseous destruction.

In the cases of sclerosing osteogenic sarcoma in the advanced stage, the "sunburst" appearance is usually seen in the roentgenogram, and above and below the region of maximum periosteal tumor formation the periosteum is raised in a characteristic manner—so-called lipping. These roentgenographic findings are the ones usually emphasized as being significant in a diagnostic sense. In the majority of cases these are not so instructive as an earlier change—evidence of sclerosis due to the formation of dense new bone which obliterates the normal markings.

The records of the cases studied in the present series reveal that sclerosing osteogenic sarcoma is frequently not diagnosed in the early stages. Two major factors contribute to these diagnostic failures. First, there is a tendency to attribute the symptoms to bursitis, neuritis

or some allied condition, and no roentgenograms are taken. Second, roentgenograms are made, but the early clouding or sclerosis in the end of the bone is either not seen, or its diagnostic significance is not recognized. The following cases are illustrative.

CASE 1.—A Negro boy aged 16 first noted pains in the right knee eight months before being examined. At first these were thought to be caused by bursitis. The pains were described as cramplike, coming on after exercise. The patient walked with a limp. Two months prior to admission to the hospital he noted a swelling along the inner portion of the leg corresponding to the region of the tibial tuberosity. The swelling grew rapidly until it reached the size of a grapefruit at the time of the patient's admission to the hospital. Examination of the region of the right knee showed a large swelling just below the knee joint which limited extension

Fig. 1 (case 1).—Roentgenogram showing sclerosis in the upper end of the tibia extending to the epiphysial line and occupying the entire breadth of the marrow cavity. The tumor extends periosteally on the medial side.

and flexion of the leg. The mass was firm and attached to bone and had several fluctuating areas. No roentgenograms had been taken. Those made after eight months of symptoms showed sclerosis and clouding of the marrow cavity in the upper third of the tibia extending to the epiphysial line (fig. 1). Radiating spicules of new bone were seen in the metaphysial region along the inner margin. Scattered areas of osseous destruction eroded the cortex and produced a mottling effect below the region of periosteal reaction. On Jan. 24, 1930, a specimen was taken from the tibia for biopsy. It disclosed numerous spindle cells and malignant osteoblasts surrounding spicules of new bone. There were occasional small giant cells. The diagnosis was osteogenic sarcoma, and an amputation through the femur at the junction of its middle and lower thirds was made on February 8.

The specimen taken from the amputated leg showed irregular areas of density in the marrow cavity toward the epiphysial line and toward the middle third of the tibia. Between these regions the bone showed necrotic tumor tissue mingled with blood occupying regions of osseous destruction. The patient died June 23, with metastasis to the lungs.

Case 2.—A white boy aged 15 was struck by a tennis racket four months prior to examination, and since that time a rather painful, fairly large tumor, about the size of half of a small orange, had developed in the region of the left knee joint. Later consolidation of one lung developed, and thoracentesis showed a small amount of bloody fluid. Prior to the recognition of the pulmonary involvement, no roentgenograms had been taken. The roentgenograms of the lung showed a massive region of increased density throughout the entire lower part of the lung, the extreme apex being relatively clear. The other lung was entirely

Fig. 2 (case 2).—Roentgenogram of the knee joint, showing sclerosis of the bone, the most prominent roentgenographic feature in this case. The first evidences of periosteal reaction are just beginning to be evident.

normal. Roentgenograms of the knee joint showed sclerosis of the marrow cavity at the upper end of the tibia and faintly radiating spicules of new bone in the periosteal region of the medial aspect (fig. 2).

Despite the fact that the symptoms were of only about four months' duration and the roentgenograms of the primary growth in the tibia showed little osseous destruction or extension of the tumor into the soft parts, the patient already had massive metastases to the lungs at the time of admission and died of pulmonary involvement four months later. No operation was performed.

Case 3.—A white girl aged 15 years struck her knee with a tennis racket, and two months later pain developed, which became localized in the upper end

of the left tibia on the inner side. The first roentgenographic examination was made two months after the onset of pain (fig. 3 *A*). The picture revealed a heavy shadow (sclerosis) in the upper end of the tibia and a small defect in the cortical bone about 2 cm. below the knee joint. The lateral view revealed some increase in density, but at the time the roentgenographic appearance was considered to be normal. A plaster cast was applied. Three weeks later a second roentgenogram showed an extension of the dense shadow, so that the entire wedge of bone along the epiphysial line to a point 4 inches (10 cm.) below had dense cloudy areas. There was little periosteal reaction, and areas of increased density were interspersed among small areas of rarefaction. On Nov. 11, 1922, an exploration was made under a tourniquet; a diagnosis of sclerosing sarcoma was made on the basis of a study of frozen sections, and an amputation was performed through the lower third of the thigh (figs. 3 *B* and 4). Pain later developed in the region

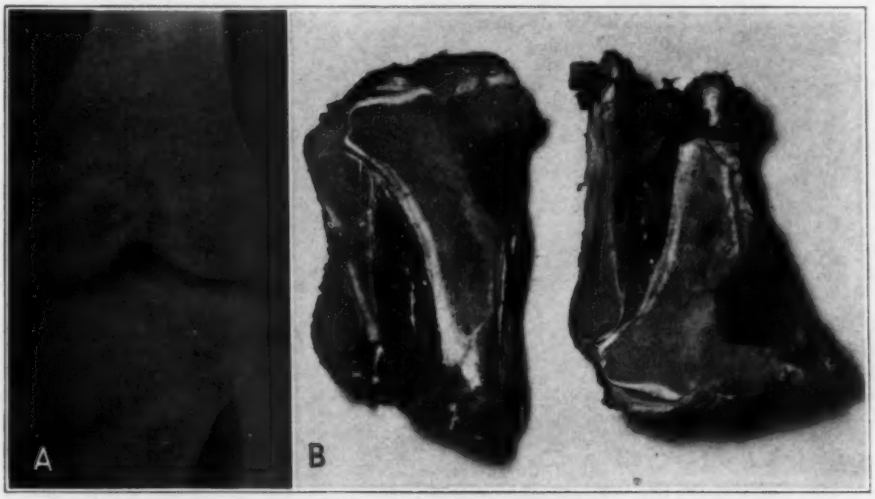

Fig. 3 (case 3).—*A*, a roentgenogram taken two months after the development of pain (the first symptom), revealing definite sclerosis in the upper end of the left tibia without any periosteal change. A biopsy was made three months after the onset of pain, and a diagnosis of sclerosing sarcoma of bone was made. An amputation was performed at the middle of the thigh. *B*, the longitudinal section of the gross specimen, showing the appearance of this type of sclerosing sarcoma.

of the spine, and fluid appeared in both sides of the chest in February 1924. The patient died of metastases in October 1924.

Variants of the sclerosing sarcoma are found in which the earliest indication of tumor formation is most marked in the subperiosteal region, and the characteristic features of a sclerosing osteogenic sarcoma are found in sections. More often, however, such a tumor contains varying amounts of cartilage and presents other transitional features, which indicates that it is related to the primary chondrosarcoma, which is in the beginning a tumor of the periosteum.

The final differentiation of sclerosing osteogenic sarcoma from other varieties of sarcoma of bone is made by microscopic examination. The former is composed of malignant osteoblasts separated by relatively large amounts of intercellular osteoid tissue. There are also found spicules of bone and spindle cells representing undifferentiated connective tissue. The irregular character of the osteoid tissue and its

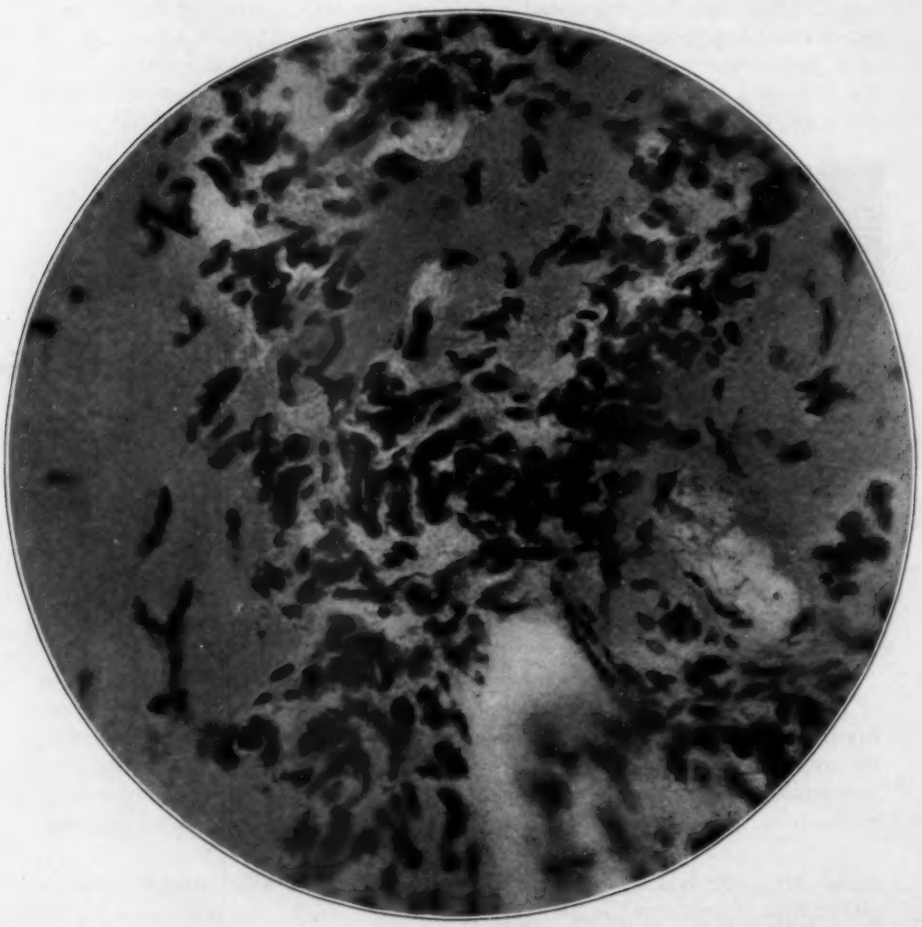

Fig. 4 (case 3).—Photomicrograph revealing the typical histologic picture of sclerosing sarcoma—malignant osteoblasts, irregular spicules of osteoid tissue and a few fibroblasts.

occurrence in all parts of the tumor in the primary growth and in metastases indicate that the osseous material is developed in the tumor (fig. 5). The tumor apparently arises from preosseous connective tissue and rapidly differentiates toward the end-product—bone.

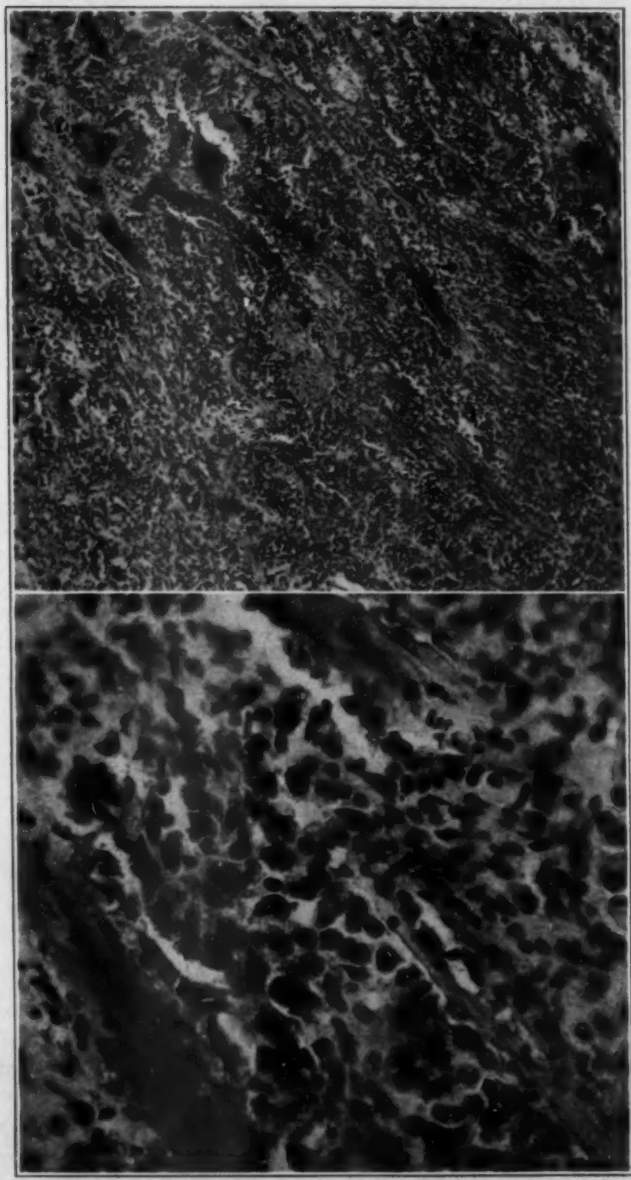

Fig. 5.—Low and high power photomicrographs of a sclerosing sarcoma, showing the proliferation of malignant osteoblasts and the formation of irregular osteoid spicules in the tumor.

PROGNOSIS

Despite the grave prognosis of sclerosing sarcoma, permanent cure is noted more frequently than in other types of sarcoma of bone. One hundred and six patients have been followed for a period of more than five years or until a fatal termination. Eighteen, or approximately 17 per cent, were living beyond the five year period, as shown in the accompanying table. Radical surgical measures were resorted to in all cases, either a resection or an amputation being performed

Fig. 6 (case 13).—Amputated specimen in a case of sclerosing sarcoma of the femur in a man aged 21. The amputation was performed by Dr. Spackman of Wilmington, Del., in April 1927. When the patient was seen in April 1937 he was entirely well. The tumor involved the entire width of the marrow cavity just above the epiphysis. There was also an extension beneath the periosteum.

(fig. 6). Resection was resorted to in the cases in which the tumor was located in the clavicle, the rib, the lower end of the humerus and the lower jaw. No cures followed irradiation. Prior to 1927, before irradiation was employed to any extent, the percentage of five year cures was nearly twice as high as in the past decade. This difference

in results is particularly striking in view of the fact that the duration of symptoms prior to treatment before 1927 averaged ten months, while during the past ten years the period averaged six months.

Data on Cases of Sclerosing Sarcoma in Which Cure Was Effected

Case	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Treatment	Result
11	W	M	17	Tibia	3½	.....	11/30/31: Amputation at middle third of thigh	Well 5 yr.
12	W	F	21	Tibia	8	Pain; swelling	April 1931: Irradiation 8/31/31: Amputation	Well 5 yr.
13	W	M	21	Femur	3½	Tumor; pain	April 1927: Amputation	Well 10 yr.
14	W	F	10	Humerus	2	Tumor; pain	7/10/25: Exploration and resection	Well 9 yr.
15	W	M	18	Femur	9	Tumor; pain	1/25/23: Amputation	Well 8 yr.
16	W	M	15	Fibula	...	.....	1/5/23: Amputation	Well 5 yr. 9 mo. later
17	W	F	38	Rib (4th)	12	Pain	12/1/21: Irradiation; amputation	Well 8 yr. later
18	W	F	19	Tibia	11	Trauma; pain; tumor	7/19/21: Exploration 7/20/21: Amputation	Well 8 yr. later
19	W	F	27	Radius	48	Fracture 4 yr.; tumor 1 ½ yr.	1/2/13: Amputation	Well almost 12 yr.; lost from observation
20	W	F	6	Femur	..	Trauma; pain; tumor; pathologic fracture	1/25/21: Aspiration; radium and irradiation 5/20/21: Amputation	Well over 9 yr.
21	W	M	15	Clavicle	3	Trauma; pain; tumor	September 1920: Resection; preoperative irradiation	Well nearly 10 yr. later
22	W	F	7	Femur	2	Tumor; trauma; pain	February 1926: Exploration; amputation	Well 6 yr.; lost from observation
23	W	M	..	Femur	..	Tumor; fracture	1/18/13: Amputation	Well over 17 yr.
24	W	F	24	Femur	18	Trauma; pain; tumor	8/8/13: Amputation	Well over 16 yr.
25	W	F	11	Tibia	1½	Tumor	May 1913: Amputation	Well over 14 yr.; lost from observation
26	W	F	25	Femur	11	Trauma; pain	9/20/21: Amputation	Dead 5½ yr. later; trouble with other leg
27	W	F	19	Femur	5	Pain; tumor	August 1919: Amputation	Dead 5 yr. later; eclampsia
28	C	F	13	Mandible	9 wk.	Tenderness; loose teeth	3/9/98: Resection	Well 25 yr. later

The average duration of life rarely exceeds fifteen months in those cases in which the treatment could not be regarded as successful. The prognosis as to permanent cure becomes progressively better when the patients remain free from metastases for eighteen months after operation.

RECURRENCE

The tumor may recur in the stump when the amputation has not been performed high enough, and recurrences in the bone considerably higher than the level of the amputation have also been recorded. The reports of several cases in which the growth recurred follow:

CASE 4.—A girl aged 17 years had had symptoms for six months, on the basis of which a diagnosis of an osteogenic ossifying sarcoma was made. In the history it is stated that a resection of the femur could have been performed but that the functional result would not have been as good as that after amputation. A high amputation was therefore performed. Tissue removed at the level of amputation revealed no evidence of tumor. According to the pathologic notes, the main mass of the tumor was outside the periosteum. At the level of the adductor tubercle

Fig. 7 (case 4).—Roentgenogram showing a dense shadow in the right side of the pelvis, the site of a huge recurrent tumor, in a patient who had a sclerosing sarcoma of the lower end of the femur.

above the medial condyle of the femur the marrow cavity was occluded. The periosteum at this level was roughened but not definitely lipped or raised. Ossification of the tumor, the age of the patient, the short duration of symptoms and the occlusion of the marrow cavity with sclerosis favored the diagnosis of osteogenic tumor of the sclerosing type. Occasionally a chondromyxoma at this site might show considerable ossification, but one would not expect so much sclerosis with involvement of the marrow cavity. The patient was operated on on Nov. 2, 1929. Roentgenograms made on May 31, 1930 (fig. 7), showed distinct evidences of recurrence, and the following note appears in the history: "This is the first time that recurrence has occurred in the stump when the resection was done through the middle of the femur." Sections of the marrow cavity were made at the time

of the amputation, and no tumor tissue was found. Within seven months the same type of tumor had recurred in the part of the shaft of the femur which was not removed. Roentgenograms of the chest were normal, but a definite ossifying mass could be demonstrated in the pelvis on the same side. We have seen masses in the groin and neck, but never a recurrence in the stump. This sarcoma ran a rapid course, terminating fatally five months after the time pain was first noted in the lower end of the right femur. A swelling could be palpated shortly after the pain appeared.

Although such a recurrence in the stump of the femur is rare after an amputation done through the middle third of the thigh for sclerosing sarcoma in the lower end of the femur and of the bones below the knee joint, local recurrence or extension in the region of the pelvis is more common in cases in which the tumor involves the upper end of the femur. In such cases amputation or disarticulation at the hip joint was formerly attempted, but without success. In the past decade no attempt at radical surgical intervention has been made in cases of sarcoma of bone in the upper third of the femur, since in the cases recorded in this laboratory for over forty years such attempts have been uniformly unsuccessful. The following history records such an unsuccessful attempt in the case of a sclerosing sarcoma in the upper third of the femur.

CASE 5.—A white youth aged 18 bruised his hip in a fall in December 1919, three months before he consulted a physician. Gradually the pain and stiffness about the hip increased. Swelling was noted, and constant pain and tenderness were experienced for three weeks. A roentgenogram revealed a density of the neck and head of the femur, with a slight periosteal reaction. On March 9, 1920, disarticulation of the hip joint was performed. When the gross specimen was examined a soft mass surrounded the neck and trochanter of the femur, which was collar shaped and covered with muscle. A cross-section of the portion of the femur involved revealed small areas of erosion in the cortical bone, and this erosion extended in places to the cartilage of the head of the bone. Areas of sclerosis were distributed among the grayish white areas of solid tumor tissue. The less dense portions were continuous with masses of tumor tissue which extended beneath the periosteum. The microscopic diagnosis was sclerosing osteogenic sarcoma of the upper end of the femur. Irregular spicules of osteoid material were distributed among solid sheets of proliferating osteoblasts. A recurrence was noted in the pelvis three months later. The patient died in July 1920, four months after the disarticulation.

INVOLVEMENT OF OTHER BONES

In some cases the question arises as to whether a second tumor is an independent growth or a metastatic one. Secondary deposits in other portions of the skeleton have been described repeatedly in cases of Ewing's tumor. In the various types of osteogenic sarcoma, however, metastasis of the tumor to other bones is extremely rare. In the

following three cases involvement of other bones in the skeleton occurred with sclerosing sarcoma primary in the lower end of the femur, the upper end of the tibia and the ilium, respectively.

CASE 6.—A white girl aged 18 injured her right leg ten months before admission to the hospital. Four months before pain and swelling appeared in the region above the knee. She continued to use the leg actively until two months before admission, when she was put on crutches to keep the leg at rest. The first roentgenograms were made after the appearance of the swelling (fig. 9). These showed a dense cloudiness in the marrow cavity of the femur extending 4 cm. above the condyle. There was an irregular periosteal reaction extending upward to about the junction of the middle third of the femur. These films were made in August 1925, and in October 1925 the sclerosis had extended up the marrow cavity of the

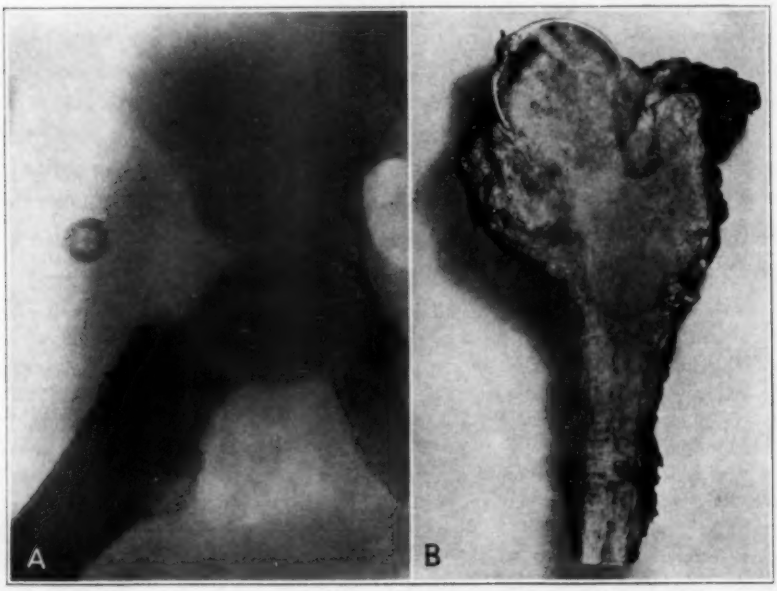

Fig. 8 (case 5).—*A*, roentgenogram, taken after symptoms of four months' duration, showing sclerosis of the marrow cavity in the neck and head of the right femur. There is a slight periosteal reaction about the neck of the femur. A disarticulation at the hip joint was performed. *B*, the gross specimen showing the extent of involvement of the upper end of the femur and the characteristic sclerosis of the marrow cavity.

femur with a large amount of new bone formation radiating at a right angle from the periosteal margin on the lateral side. The diagnosis on the basis of the roentgenographic picture was sclerosing osteogenic sarcoma. On October 28 Dr. Bloodgood performed an amputation through the middle of the right thigh. The lesion was explored before amputation, and frozen section confirmed the diagnosis of sarcoma. In January 1926 a bony swelling appeared in the region of the hyoid bone in the neck, which was attached to the hyoid bone and seemed fixed to the larynx. In April 1926 fluid was found in the pleural cavities. The patient died of pulmonary metastases on May 29.

CASE 7.—A white boy aged 11 years fell and injured his right knee in September 1933. A large black and blue area developed on the inner surface of the knee. Cold applications were applied, but the bluish discoloration did not disappear. There was no pain or swelling. The discoloration persisted for about one month and then cleared. During this time there was no loss of function of the right leg. About nine weeks before the present examination the patient commenced to limp. There was no swelling or pain in the leg. However, the patient complained of fatigue in each leg. One week later a swelling was noticed which was not discolored nor tender and seemed to have normal resistance. The limping continued, and the patient then noticed pain in the right leg on arising, which would disappear during the day. The swelling increased slightly. The patient was seen by a physician, who referred him to the hospital for application of a cast. This was done five weeks before our examination. At that time a diagnosis of subacute

Fig. 9 (case 6).—Roentgenograms showing sclerosis of the marrow cavity in the lateral view and periosteal extension of the tumor along the lateral margin of the lower end of the femur in the anteroposterior view.

osteomyelitis was made. The lesion was explored and curetted in June 1934. After the exploration the tumor grew rapidly, and the newly formed bone grew through the periosteum and extended into the soft parts (fig. 10). A diagnosis of osteogenic sarcoma was made, and an amputation was done in July 1934 through the thigh. After amputation the patient complained of severe pain and stiffness in the right arm. For a while no attention was paid to these symptoms, but in 1935 a roentgenogram disclosed a dense shadow in the right humerus in the same position as in the tibia at the diaphysial end of the bone, and in February 1936 the typical picture of a sclerosing sarcoma was found. In April 1937 the lesion in the shoulder is much larger, and the boy is rapidly losing ground (fig. 11).

Fig. 10 (case 7).—Roentgenograms showing a sclerosing sarcoma of the upper end of the tibia.

Fig. 11 (case 7).—*A*, a roentgenogram, taken in 1935, showing sclerosis of the marrow cavity in the neck of the humerus. *B*, a roentgenogram, taken in April 1937, showing extensive periosteal reaction and invasion of the soft parts. The patient was referred by Dr. T. P. Loughery, of Germantown, Pa.

CASE 8.—A white man aged 61 had no complaints except that of pain in his hip. On examination large palpable bony tumor masses were found in the region of the ilium over the sternum and ribs, and several nodular masses were felt protruding in the region of the calvarium (fig. 12). A specimen for biopsy was taken from the tumor in the sternum. The histologic structure was that of a typical sclerosing sarcoma. The tumor in the pelvis grew rapidly, and the patient died six months after the biopsy was done.

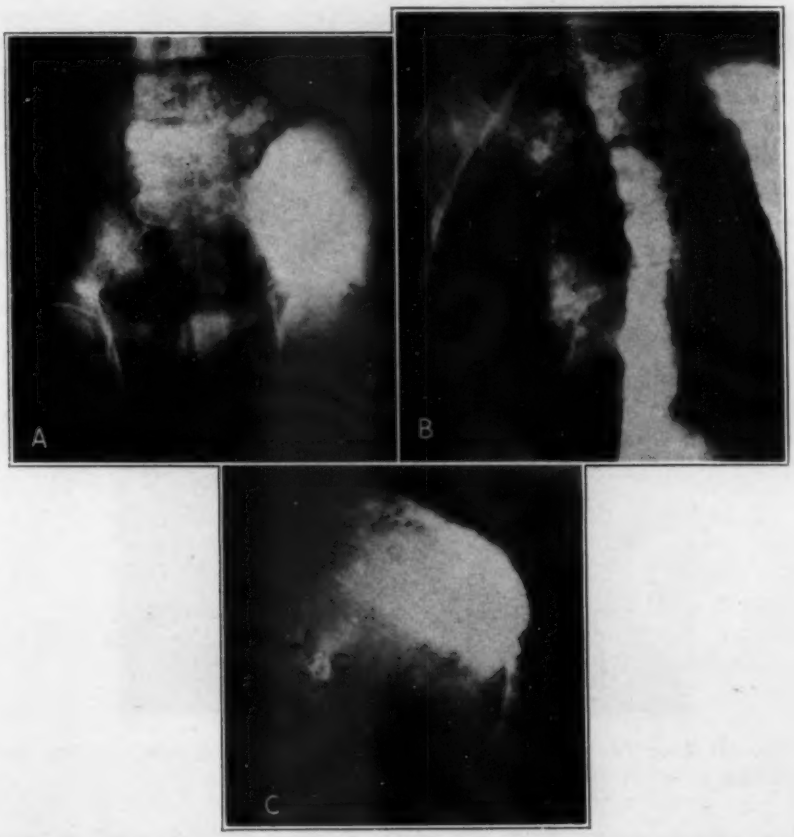

Fig. 12 (case 8).—Roentgenograms showing tumor masses in the right side of the ilium (*A*), the third and fourth ribs (*B*) and in the calvarium (*C*). The patient was referred by Dr. J. Atlee, Lancaster, Pa.

IRRADIATION

Sclerosing osteogenic sarcoma is not a radiosensitive tumor. However, in cases of inoperable tumor in which pulmonary metastases have already occurred, when the tumor is situated in the bones of the pelvis or in the upper end of the femur, high voltage roentgen therapy may lessen the swelling and decrease the pain for several months. We have

no proof to date that irradiation will prolong life or cure the disease, and our evidence is not in favor of preoperative irradiation. Sometimes irradiation must be resorted to when consent for radical surgical intervention cannot be obtained.

CASE 9.—A white woman aged 23 was perfectly well until July 1931, when she began having what seemed to be sciatic rheumatism on the left side. She was treated for neuritis and arthritis until three weeks before the present examination. There were localized tenderness and pain over the left sacro-iliac joint, tenderness along the sciatic nerve and secondary scoliosis with convexity of the curve away from the side of the lesion. A tumor occupied a large part of the left lower quadrant, extending up to a point midway between the ilium and the umbilicus. The mass was found to be tender to pressure, and the pain was localized in the sacro-iliac area, traveling down the sciatic nerve. The roentgenogram showed a

Fig. 13 (case 9).—Roentgenogram showing an ossifying tumor in the right side of the pelvis in the region of the sacro-iliac joint.

sclerosing tumor occupying the left side of the ilium and the sacro-iliac region (fig. 13). There was much new bone formation with some radiating spicules. The patient was treated with high voltage roentgen radiation in 1933 and 1934. The pain was somewhat relieved for a period of three months, but the growth of the tumor continued. The patient died of metastasis to the lungs early in 1935.

CASE 10.—A white man 23 years of age injured the lower part of the femur on the inner aspect four months before examination. The diagnosis of a strained ligament was made by the family physician. One month before examination considerable pain was experienced, with some limitation of motion. At the time of examination considerable enlargement of the right knee was noted, the circumference measuring 45 cm. The skin over the swelling was tense and red; the swelling was tender. On roentgen examination a dense shadow was found in the marrow cavity, which extended throughout the lower third of the femur to the articular

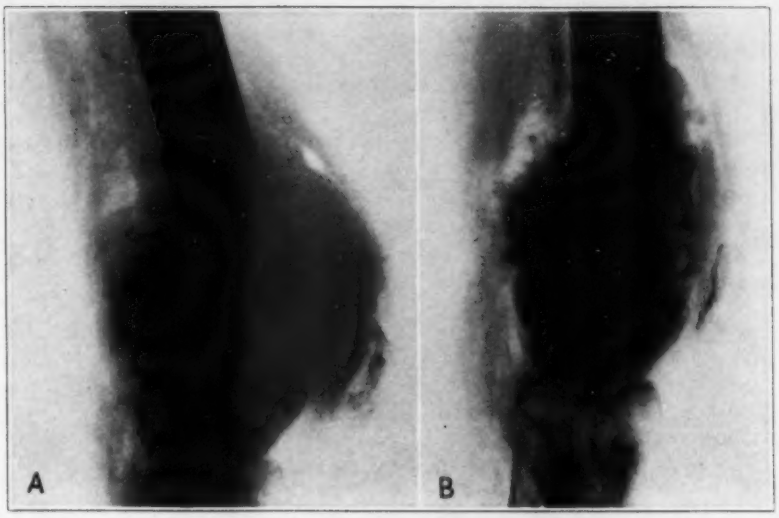

Fig. 14 (case 10).—*A*, a roentgenogram taken in October 1934, which formed the basis for a diagnosis of osteogenic sarcoma. The tumor filled the marrow spaces at the lower end of the femur and extended beneath the periosteum. There was a large soft part shadow above the patella. Between October 1934 and February 1935 the patient received high voltage roentgen therapy—a total dose of 3,840 roentgens. The swelling receded, and the pain was relieved. The ossifying mass, however, was not decreased in size, as shown in *B*.

Fig. 15.—Roentgenogram showing characteristic sclerosis in the lower end of the radius, produced by a sarcoma. The swelling was of only seven weeks' duration at the time this film was taken. There was little periosteal tumor reaction. Compare with figure 16.

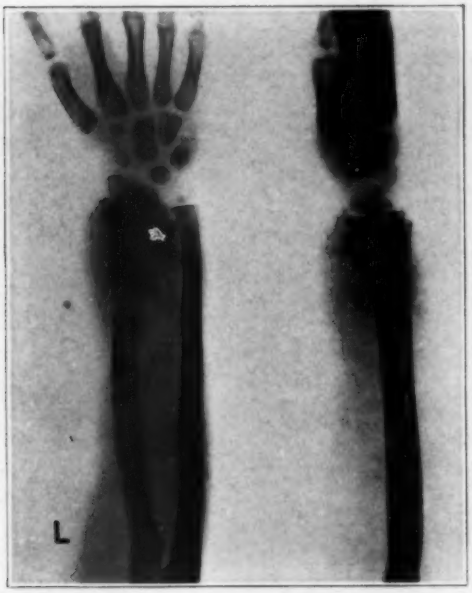

Fig. 16.—Roentgenogram of a sarcoma of the lower end of the radius of the patient shown in figure 15. This film was made one month after figure 15 and only eleven weeks after the onset of symptoms. There was a pronounced periosteal reaction, and the bulk of the tumor was outside the bone. The characteristic sunburst appearance was present.

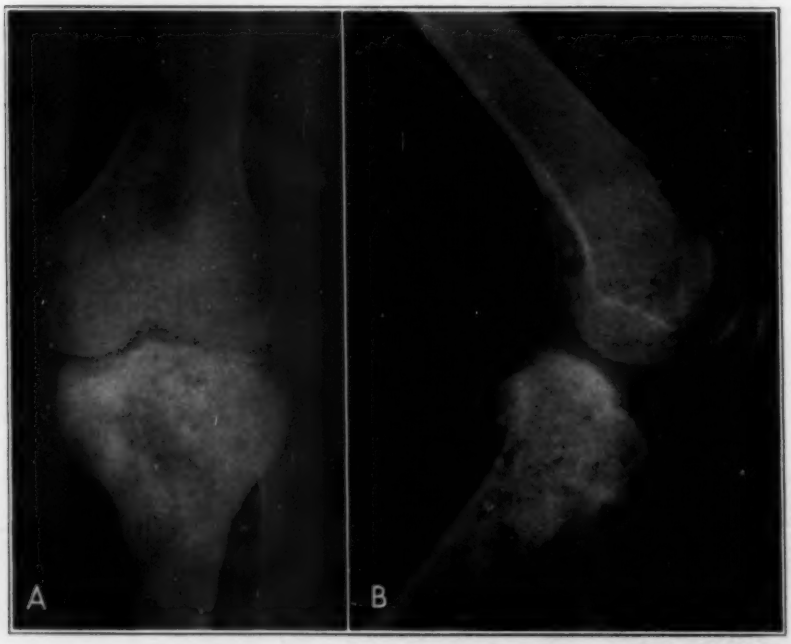

Fig. 17.—Roentgenograms of a sclerosing sarcoma three months after the onset of symptoms. The tumor invaded the cortical substance and cancellous bone throughout the upper end of the tibia extending to the joint surface. In spite of the extensive involvement of bone, there were relatively little periosteal reaction and practically no invasion of the structures surrounding bone.

cartilage (fig. 14). No periosteal lipping was noted. Just above the internal condyle the cortical bone was eroded. Shadows of masses, apparently dense, were visible in the soft parts along the sides of the femur. Since the patient's family would not consent to amputation, high voltage roentgen therapy was employed. Between October 1934 and February 1935 a total dose of 3,840 roentgens in divided doses over three fields was given. The pain was relieved, and the swelling about the knee was reduced. Despite these indications of improvement, the shadows increased decidedly. The patient died about six months after treatment was begun

Fig. 18.—Roentgenogram of the knee joint of a white youth aged 20, who during May 1936 felt some pain in the right tibia just below the knee. The pain seemed worse at night. In December 1936 he visited a physician, and a diagnosis of tumor of the bone was made. Roentgen treatments were then started, the skin later becoming red and discolored. After the treatments the swelling had decreased somewhat. The patient lost 30 pounds (13.6 Kg.) during a short time. No metastases to the lungs were found. In the roentgenograms the lateral portion of the head of the tibia is sclerosed. The tumor has not invaded the soft parts, and there is no periosteal "sunburst." An amputation was performed through the middle of the thigh. Microscopically, variations and pleomorphism were noted in the cell structure, as well as the presence of large amounts of osteoid tissue. The tumor, however, on the whole was not very cellular, and new bone formation predominated.

COMMENT

A careful study of sclerosing osteogenic sarcoma in its earliest phases indicates that the most characteristic location of the tumor is neither in the periosteum nor in the subperiosteal regions but in the bone itself in its cancellous or cortical portions. The characteristic sunburst and periosteal manifestations so often stressed as diagnostically significant in the roentgenogram are late manifestations. Because of the rapid growth of the tumor, this mode of onset is often obscured.

Fig. 19.—Roentgenogram of a typical sclerosing sarcoma in the lower end of the femur in a boy aged 10. The dense triangle of new bone has the characteristic location of the shaft side of the epiphysial line. There is a beginning periosteal reaction.

The tumor shown in figures 15 and 16 illustrates this point. In this case the tumor arose in the lower end of the left radius in a child of 7. The swelling was only of seven weeks' duration when the first roentgenogram was made on April 26, 1926 (fig. 15). In this film the metaphysis of the lower end of the radius is sclerosed, and there is little periosteal new bone. In the film made one month later, May

28, 1926, the characteristic sunburst of periosteal new bone is seen (fig. 16). In this case had the roentgen examination been postponed for a matter of a few weeks only, the origin of the tumor in the substance of the bone proper would not have been suspected.

From the standpoint of the histogenesis of the tumor it is not easy to decide whether this early manifestation within the bone, as seen in the roentgenogram, is due to the origin of the tumor in this region or to the fact that the tumor tissue invading bone tends to ossify earlier when there is an abundant supply of mineral salts furnished by normal bone. That the tumor may begin in bone is indicated by cases in which the bulk of the tumor is confined to bone in the relatively advanced stages. Such a case is illustrated in figure 17, which shows fairly extensive involvement of the head of the tibia with relatively little periosteal reaction. Similar cases are illustrated in figures 18 and 19. The histologic structure of the tumor also suggests such an origin. In young persons ossifying sarcoma begins beneath the periosteum, and cartilage arising from remnants of the primitive perichondrium is often found in the tumor. In adults ossifying sarcoma may develop from the region of the periosteum, and when this occurs the bulk of the tumor is usually found outside the bone. The histologic structure of these periosteal tumors in adults differs from that of typical sclerosing sarcoma in containing large amounts of fibrous tissue. In contrast to this, malignant osteoblasts and osteoid spicules usually predominate in the section from a typical sclerosing sarcoma.

TORSION OF THE FALLOPIAN TUBE IN THE VIRGIN

REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Torsion of the fallopian tube is not an exceedingly rare condition. Since the first report of a case by Bland-Sutton [1] in 1890, followed by one by Delbet [2] in 1892, there have appeared reports of many cases in which the torsion was due to various pathologic conditions of the adnexa (pyosalpinx, hydrosalpinx, hematosalpinx and tumor). In many cases torsion of the tube was associated with torsion of the corresponding ovary. Anspach,[3] who reviewed the literature in 1912, collected reports of eighty-five cases of torsion of the diseased tube. In most cases the tube was transformed into a cystic tumor, thus creating conditions that favor its twisting around the pedicle. Eastman [4] in 1927 reviewed the literature on torsion of hydrosalpinx. This kind of torsion of the pathologic tube is referred to in the German literature as *Tubenstieldrehung* in contrast to *Tubentorsion,* which means torsion of the previously normal tube. These terms may be translated into English as "torsion of the tubal pedicle" and "torsion of the tube." This distinction, which appears to us essential, is based on the fact that the normal fallopian tube does not possess a proper pedicle, and the existence of a pedicle is identical with the cystic transformation of the tube (hydrosalpinx and pyosalpinx).

Torsion of the undiseased fallopian tube is of much rarer occurrence. The first observations of torsion of normal adnexa in a virginal genital

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1. Bland-Sutton, T.: Salpingitis and Some of Its Effects, Lancet **2**:1146-1148 and 1206-1209, 1890.

2. Delbet, P.: Torsion du pédicule dans un cas de salpingite, Bull. Soc. anat. de Paris **67**:300-302, 1892.

3. Anspach, B. M.: The Torsion of Tubal Enlargements with Especial Reference to Pyosalpinx, Am. J. Obst. **66**:553-595, 1912.

4. Eastman, N. J.: Torsion of Hydrosalpinx, Surg., Gynec. & Obst. **45**:143-147, 1927.

tract were reported by Stark [5] in 1911, Norris [6] in 1911, Cassidy and Norbury [7] in 1911, Auvray [8] in 1912 and 1913 and Schweitzer [9] in 1918.

Stark observed torsion of the left tube in a 46 year old virgin. Her past history was essentially irrelevant. She was suddenly taken ill with a severe attack of abdominal pain localized in the left iliac region. When the abdomen was opened a few blood clots were found lying loosely in the pelvis. The left tube was twisted into three complete turns from right to left. On the right side a dermoid cyst with sebaceous material and hairs was found. Microscopic examination did not reveal any signs of pregnancy. The case of Norris was that of a 19 year old virgin. There was complete torsion of the right ovary with secondary involvment of the tube. Cassidy and Norbury reported a case of torsion of the entire left adnexa in a girl 11 years old. In 1912 Auvray wrote a monograph on torsion of the normal adnexa and reported a case of torsion of the right normal tube and ovary in a girl 14½ years old. In 1913 he published the report of a case of isolated torsion of the right tube in a virgin 28 years old. For two years at intervals she complained of cramplike pains in the right lower abdominal quadrant. At operation a mass the size of a tangerine was found in the pelvis. The tip of the appendix was attached to the mass, which consisted of the right tube twisted twice and distended with bloody fluid. The ovary and the opposite adnexa were normal. Pathologic examination revealed mainly extensive necrosis and hemorrhage. In the less affected areas there were some inflammatory changes consisting mainly of accumulations of round cells and occasional giant cells. These changes were considered secondary. The appendix was undiseased. In 1918 Schweitzer called the attention of the German medical profession for the first time to torsion of a normal tube. His case was that of a single girl 21 years old. (For details, see case 2 in the table.) In the ten years from 1908 to 1918 Schweitzer could not find a similar case in the large material of the University Clinic of Leipzig. We found only occasional similar reports in the following years up to about ten years ago. Since this time the medical literature shows an increasing number of reports dealing

5. Stark, J.: Acute Torsion of Normal Appendages with Hematosalpinx, J. Obst. & Gynæc. Brit. Emp. **19**:258-260, 1911.

6. Norris, C. C.: Torsion of the Normal Uterine Appendages: Report of a Case, Am. J. Obst. **63**:850-854, 1911.

7. Cassidy, M. A., and Norbury, L. E. C.: Torsion of the Left Broad Ligament and Fallopian Tube in a Child, Lancet **1**:98-99, 1911.

8. Auvray, M.: (*a*) De la torsion spontanée de la trompe et de l'ovaire normaux, Bull. Soc. d'obst. et de gynéc de Paris **1**:727-731, 1912; (*b*) Nouveau cas de torsion spontanée de la trompe saine, Arch. méns. d'obst. et de gynéc. **2**:97-104, 1913.

9. Schweitzer, B.: Isolierte Torsion der normalen Tube, Zentralbl. f. Gynäk. **42**:25-33, 1918.

Year	Author	Age of Patient	Clinical History	Preoperative Diagnosis	Operative Findings	Pathologic Examination
1913	Auvray [8b]	28	Cramplike pains in right lower abdominal quadrant at intervals for 2 yr.; last attack more severe; temp. 39 C. (102.2 F.); menses since 14 yr.; fairly regular; dysmenorrhea for past 6 mo.; past history irrelevant	Appendicitis	Mass about the size of a tangerine in pelvis; right tube twisted twice and distended with bloody fluid; tip of appendix attached to mass; ovary and opposite adnexa normal	Marked necrosis and extensive hemorrhages; some inflammatory changes in less destroyed areas; many round cells and occasional giant cells; no polymorphonuclears; inflammatory changes considered secondary; ovary and appendix normal
1918	Schweitzer [9]	21	Sudden onset of severe pain in lower part of abdomen; painful micturition; 5 wks. later similar attack at menstruation	Twisted ovarian cyst	Left adnexa: cystic tumor, size of an apple, bluish red, in adhesions with omentum and lateral abdominal wall; left tube twisted twice in middle portion; ovary normal; right adnexa: tube about twice normal length; otherwise normal	Severe circulatory disturbances; diffuse hemorrhagic infarction of wall of tube; venous circulation particularly affected; veins and capillaries maximally distended and partly ruptured; sactosalpinx haemorrhagica Cause: torsion of tube
1922	Hansen [20]	14 Not yet menstruating	Sudden onset of severe pain in right lower abdominal quadrant; first attack after exercise; vomiting; tenderness and rigidity; W. B.C. 30,000; temp. 37.8 C. (100 F.); past history irrelevant	Appendicitis with abscess formation	Torsion of right tube in its isthmic portion (360 degrees); tube tense, the size of a hen's egg and bluish black; fimbriated end closed; small follicular cyst on ovary; opposite adnexa normal; appendix long and thickened in distal position	Not reported
1925	Davies [18]	19	Acute pain in right iliac fossa; continuous vomiting; patient menstruating the day of incident	.....	Appendix slightly congested; right tube black and swollen to size of small victoria plum; twisted clockwise; mesosalpinx abnormally long; both ovaries normal	No histologic report; blood clot in lumen of tube; wall congested and thickened; hemorrhages into wall; no evidence of inflammation
1925	Rogers [19]	16	Acute pain in lower part of abdomen of 1 days' duration; vomiting	.....	Ampullary portion of right tube black, swollen and twisted on its mesosalpinx; left tube also underwent torsion but to a less extent	Dense hemorrhage in which remains of wall of tube could be seen
1926	Darner [16]	13	Sudden onset of colicky pain in right iliac fossa; nausea; no vomiting; rigidity and tenderness in entire right lower quadrant; W.B.C. 14,800; menstruation began 2 mo. before hospitalization; since then amenorrhea	Acute appendicitis with abscess	300 cc. of a blood-tinged fluid in peritoneal cavity; appendix normal; distal third of right tube greatly distended and bluish black; fimbriae markedly swollen; small hydatid cyst attached to mass; medial and proximal third of tube twisted clockwise 3½ times; ovary and opposite adnexa normal	Serosa completely disappeared; muscularis infiltrated with fresh and old hemorrhages; veins markedly dilated; marked edema; degeneration of epithelium; tubal lumen extremely dilated and filled with blood clots; no evidence of fresh or old inflammatory lesion; appendix normal
1926	Gillies [23]	23	Acute pain in left iliac fossa; vomiting; pain on micturition for 3 days	Appendicitis (most probable)	Abundant free fluid in pelvis; left tube swollen, nearly black and twisted twice around its long axis; ovary and right adnexa normal	No report
1927	Fiolle [12]	10 Not yet menstruating	Sudden onset of severe pain in lower part of abdomen; vomiting; tenderness throughout abdomen, most marked in right iliac fossa; temp. 37.1 C. (98.8 F.)	Appendicitis with perforation (?)	Abundant free blood in peritoneal cavity; appendix long and slightly injected; at right of uterus a black mass the size of a tangerine attached to a pedicle, distinctly twisted twice clockwise	Grossly, no morphologic details recognizable (blood clots); microscopically, mostly necrotic tissue; abundant leukocytic infiltration; in less destroyed places, epithelium resembled that of the tube
1928	Vighold: Acta obst. et gynec. Scandinav. 7:310-322, 1928.	17	Sudden onset of abdominal pains in right iliac fossa; no nausea or vomiting; [illegible] ney's point; temp. 38.2 C. (100.7 F.); menses since 16 yr.	Acute appendicitis	Appendix normal; orange-sized tumor of tube twisted 3 times clockwise around its pedicle; no adhesions; ovary and left adnexa normal	Grossly, tube not recognizable; tissue soaked with blood; blood vessels distended; some small groups of lymphocytes; peritoneal endothelium well preserved; mucosa not recognizable; diagnosis: stasis permagna tubae cum haemorrhagia
1929	Koster [17]	16	Sudden sharp pain in lower part of abdomen; frequent micturition; no nausea or vomiting; menses since 14 yr.; dysmenorrhea; menstruation at time of torsion	Ovarian cyst with twisted pedicle	Serosanguineous fluid in peritoneal cavity; right tube twisted 1½ turns on the inner 3d; distal to [illegible] tube swollen, bluish black and tense; fimbriated end free; left adnexa and appendix normal	Fibrous tissue and muscle bundles separated by multiple hemorrhages; veins distended; mucosa unrecognizable; diagnosis: hemorrhagic infarction
1929	Gabe [13]	13	Dull pain across lower part of ab-	Acute	Free blood-tinged fluid; appendix;	Extravasation of blood into the

	ney's point; temp. 38.2 C. (100.7 F.); menses since 16 yr.				adhesions; ovary and left adnexa normal	thelium well preserved; mucosa not recognizable; diagnosis: stasis permagna tubae cum haemorrhagia
1929 Koster [17]	16	Sudden sharp pain in lower part of abdomen; frequent micturition; no nausea or vomiting; menses since 14 yr.; dysmenorrhea; menstruation at time of torsion	Ovarian cyst with twisted pedicle	Serosanguineous fluid in peritoneal cavity; right tube twisted 1½ turns on the inner 3d; distal to this point tube swollen, bluish black and tense; fimbriated end free; left adnexa and appendix normal	Fibrous tissue and muscle bundles separated by multiple hemorrhages; veins distended; mucosa unrecognizable; diagnosis: hemorrhagic infarction
1929 Gabe [15]	13	Dull pain across lower part of abdomen; nausea and vomiting; W.B.C. 18,000; temp. 100 F.; marked tenderness over McBurney's point; menses since 11 yr.; fairly regular	Acute appendicitis	Free blood-tinged fluid; appendix; old adhesions, not inflamed; right tube size of an orange, twisted 2½ turns (4 cm. from uterus); ovary and left adnexa normal	Extravasation of blood into the tissues due to mechanical strangulation; no evidence of organic disease (3 photomicrographs)
1929 Debray: Ann. d'anat. path. **6**: 1255-1256, 1929	15½	Attack of severe abdominal pains in right iliac fossa at end of regular menstrual period; past history unimportant	Acute appendicitis	Some serosanguineous fluid in the cavity; right tube twisted 3 times clockwise; appendix slightly injected; ovary and left adnexa normal	Normal portion of the tube near uterus; zone of torsion; external portion consisting of black, markedly swollen tubal mass; fimbriae thickened but recognizable, contain a small hemorrhagic cyst; ostium patent; blood clots; no evidence of old or recent inflammatory lesions
1930 Walawelski: Zentralbl. f. Gynäk. **54**: 861-867, 1930	21	Since childhood occasional pains in lower part of abdomen; severe attacks independent of menstruation of 1 year's duration; menses since 17 yr.	Appendicitis	Apple-sized bluish tumor, cystically distended; right tube twisted clockwise 360 degrees	Tissue of the tube histologically normal in places; in other places, complete hemorrhagic infarction
1932 Sorrel, Oberthur and Loutsch: Bull. et mém. Soc. nat. de chir. **58**: 909-913, 1932	13	Several attacks of abdominal pains and vomiting; first attack at onset of menstruation 3 mo. previously; past history, appendicitis with abcess and spontaneous resorption when 9 yr. old	Appendicitis; torsion of adnexa (?)	Serosanguineous fluid in peritoneal cavity; appendix normal; black mass in cul-de-sac consisting of distended and contraclockwise twisted right tube; ovary and left adnexa normal	Histologic picture confirmed gross findings that tube was not diseased
1932 Ricard [28]	14	Severe attack of pain in right lower quadrant repeated the following day with vomiting; temp. 38.2 C.; diffuse tenderness and rigidity; menses regularly since 5 months before present illness	Acute appendicitis	Abundant serous, slightly bloody fluid in peritoneal cavity; appendix swollen, injected and definitely diseased; right tube distended and twisted 4 times in its ampullar portion, forming a black mass; ovary and left adnexa normal	Layers of the wall dissociated by a recent hemorrhage; on the surface numerous accumulations of red blood cells; no evidence of old or recent inflammatory process
1932 Caucci [31]	19	Sudden onset of pain in left lower quadrant; vomiting; temp. 38 C. (100.4 F.)	Torsion of left ovarian cyst	Distended infarcted left tube twisted in its ampullar portion twice contraclockwise; appendix injected; ovary and right adnexa normal	Lesions of a hemorrhagic infarction; no evidence of previously existing pathologic process
1933 Block and Michael [30]	13 not yet menstruating	Awakened from sleep by sharp pain in left lower quadrant; nausea; vomiting one hour later; W.B.C. 15,000; 82% polymorphonuclears; no fever; past history unimportant	Acute appendicitis	Small amount of free blood in peritoneal cavity; appendix fairly normal; right tube dark red, gangrenous and size of a hen's egg; twisted 2½ turns contraclockwise; left adnexa normal	Almost total destruction of mucosa of tube; edema and hemorrhages of the wall; blood vessels engorged; large area of blood clots; picture that of cellular destruction due to strangulation rather than inflammatory process
1934 McEachern: Brit. M. J. **1**: 190-192, 1934	14	Pains in right lower quadrant of 4 days' duration; vomiting; temp. 98.8 F.; attacks of pain in right iliac fossa since age of 2; menstruated 3 times; fourth menses appeared 24 hr. after operation	Acute appendicitis	Right tube much enlarged; twisted 2 complete turns in anticlockwise direction; hemorrhagic effusion into wall and lumen; ovary not involved; appendix mildly inflamed	Hemorrhagic effusion as the result of torsion; no evidence of pregnancy
1935 Lepoutre: Bull. Soc. d'obst et de gynéc. **24**: 388-389, 1935	15	Sudden onset of severe abdominal pain in lower left quadrant; nausea; bile vomiting; abdomen slightly rigid; tender throughout; menses appeared shortly after operation	Torsion of left ovarian cyst	Left tube black and twisted 2 complete turns; ovary not involved in torsion; contains small cysts; right adnexa normal	Abdominal ostium of the tube patent; histologic examination not reported

with torsion of the undiseased adnexa. Especially numerous are the reports of French authors, who consider torsion of normal tubes a definitely established clinical and pathologic entity of more frequent occurrence than is usually thought of (Auvray,[8] Michon,[10] Caraven,[11] Fiolle [12] and others). Most of these cases occurred in virgins. Together with Gabe,[13] we wish to make a sharp distinction between the tube of a virgin and that of the married woman. Beyond the state of virginity and after abortion, pregnancy or the puerperium there are too many possibilites of infection (specific and nonspecific) and mechanical derangements which may have an effect on the structure and the function of the tube. They render the exact determination of the "normality" of the twisted tube impossible. On the other hand, the mere fact of virginity is not sufficient evidence that the tube was undiseased before torsion. In fact, Anspach collected reports of thirteen cases of torsion in nonmarried women ranging in age from 18 to 49. On operative inspection or histologic examination, all the tubes showed marked pathologic changes other than those due to torsion. In the reports of four cases we found the remark "virgin"; in others, only "single" or "unmarried." Anspach expressed the belief that torsion of a normal tube is impossible and that in cases of torsion in which the tube appears to be normal the condition is the result of an unrecognized salpingitis and hydrosalpinx following an acute exanthema, vulvovaginitis or an attenuated tuberculosis in childhood. In recent time Thorek [14] supported this view by presenting the report of a case of torsion of the right fallopian tube in a 14 year old girl who was a virgin. At operation the periappendical structures, the parovarium and the right tube were found to be inflamed. The left ovary was greatly enlarged and cystic. Sections from the tube showed chronic and subacute salpingitis. In reporting this case, Thorek stated that few such cases had been described in the literature. In fact, in most of the cases of twisted virginal tubes the existing pathologic process was considered merely the result of torsion and strangulation.

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10. Michon, L.: Le volvulus des annexes saines (à propos de 5 cas personnels), Gynéc. et obst. **21**:103-119, 1930. Michon, L., and Trillat, P.: Volvolus d'une annexe saine, Lyon chir. **28**:648-651, 1931.

11. Caraven, J.: Torsion des annexes normales avec hématocèle pelvienne, Bull. et mém. Soc. nat. de chir. **53**:550-558, 1927.

12. Fiolle, J.: Torsion annexielle avec inondation péritonéale hémorrhagique chez une enfant de dix ans. (A propos de la valeur diagnostique de la contracture abdominale), Bull. et mém. Soc. nat. de chir. **53**:1238-1241, 1927; Torsion des annexes saines, ibid. **55**:785-787, 1929.

13. Gabe, W. E.: Torsion of the Undiseased Fallopian Tube, Arch. Surg. **18**: 1304-1314 (April) 1929.

14. Thorek, M.: Torsion of Fallopian Tube in Virgin, M. J. & Rec. **125**:470-473, 1927.

Marked disagreement prevails among the authors as to the real frequency of torsion of an undiseased tube. In 1921 Smith and Butler [15] were able to collect reports of only fourteen cases of torsion of normal adnexa in females at any age and only three cases of the isolated torsion of a normal tube in nulliparous women (Stark,[5] Auvray,[8] Schweitzer [9]). Darner [16] in 1926 reported a case of torsion of a normal fallopian tube in a 13 year old girl. Reviewing the literature, he found reports of only twelve cases of torsion of a normal tube in females at any age. Only five of them occurred in women who had never been pregnant. Darner considered primary torsion of the normal tube an "exceedingly rare" condition. In 1929 Koster [17] found reports of eleven authentic cases of primary torsion of supposedly normal tubes in nulliparous women (Davies,[18] Auvray,[8] Schweitzer,[9] Rogers,[19] Hansen,[20] Stark,[5] Darner,[16] Jefferson,[21] Gillies,[22] Gabe [13] and Heil [23]). Even a few of these cases appear to us questionable, and the case of Heil does not belong in this group. In Heil's case the ovary was involved in the torsion, and on the opposite side there was a dermoid cyst with beginning torsion of the pedicle.

Downer and Brines [24] were able to find in the literature in 1931 reports of only six cases of twisted, otherwise normal fallopian tubes (Schwartz,[25] Koster,[17] Hansen,[20] Rogers,[19] Darner [16] and Gabe [13]). We would exclude from this list the case of Schwartz, since in his case (that of a girl 16 years old) the opposite left tube was not normal. Its distal end was cystically distended, so that a bilateral salpingectomy was required. Shute,[26] who in 1932 commented on cases of adnexal

15. Smith, R. R., and Butler, W. J.: Concerning Torsion of the Uterine Adnexa Occurring Before Puberty, Am. J. Obst. & Gynec. **2**:507-521, 1921.

16. Darner, H. L.: Torsion of the Normal Fallopian Tube, Am. J. Obst. & Gynec. **11**:368-377, 1926.

17. Koster, H.: Torsion of Normal Fallopian Tube, Am. J. Surg. **7**:67-74, 1929.

18. Davies, D. J.: Torsion of Fallopian Tube, Brit. M. J. **1**:657, 1925.

19. Rogers, L.: Torsion of Fallopian Tube, Brit. M. J. **1**:778, 1925.

20. Hansen, A.: Tubentorsion mit Haematombildung und ihre Aetiologie, Zentralbl. f. Gynäk. **46**:707-708, 1922.

21. Jefferson, J. C.: Torsion of Fallopian Tube, Brit. M. J. **1**:55, 1926.

22. Gillies, J. C.: Torsion of Fallopian Tube, Brit. M. J. **1**:187, 1926.

23. Heil, K.: Ein Fall von Stieldrehung der Tube bei virginellem Genitaltraktus, Zentralbl. f. Gynäk. **45**:498-499, 1921.

24. Downer, F. G,. and Brines, O. A.: Torsion of Undiseased Uterine Adnexa in Virgins, Am. J. Obst. & Gynec. **21**:665-671, 1931.

25. Schwartz, J.: Beitrag zum Vorkommen der Eileiterdrehung, Zentralbl. f. Gynäk. **46**:1959-1961, 1922.

26. Shute, E.: Comments on Torsion of Adnexa: Report of Illustrative Cases, Am. J. Surg. **16**:490-500, 1932.

torsion under every condition, reported six cases of his own. He stated that in fifty-three reported cases fairly good evidence was found that the tube involved was normal.

Regad [27] published several instructive and complete expositions on this subject and in 1933 summarized his conclusions based on the two hundred and one cases reported up to date, as shown in the following tabulation:

Relative Frequency of Torsion of the Fallopian Tube

Torsion of undiseased tube	24	per cent
(Histologic examination in only 8 per cent)		
Torsion of the hydrosalpinx	18	per cent
Torsion in hernial sac	14	per cent
Torsion of salpingitis, tubal pregnancy or twisted tumor	13.5	per cent
Torsion in the course of pregnancy	12	per cent
Torsion associated with appendicitis, fibromas or cyst of the ovary	9.5	per cent
Torsion followed by spontaneous amputation	5	per cent
Torsion, bilateral (diseased and undiseased)	4	per cent

Frequency According to the Genital Activity

Before puberty	20	per cent
During the genital activity of women	80	per cent
These 80 per cent are distributed as follows:		
Virgins	33	per cent
Nulliparous women	25	per cent
Pregnant women	24	per cent
Multiparous women	18	per cent

Frequency According to the Age

In babies and infants	5	per cent
Between 10-13 years	16	per cent
Between 13-22 years	44	per cent
Between 22-35 years	25	per cent
Between 35-49 years	10	per cent

Side Affected		Kind of Torsion	
Right	68 per cent	Clockwise on the right side	62 per cent
Left	32 per cent	Anticlockwise on the left	38 per cent

Mosettig [28] reviewed the German literature in 1933 and traced fourteen cases of torsion of a supposedly normal tube. Of these, only the cases of Schweitzer,[9] Hansen [20] and Rueder [29] occurred in a virginal genital tract.

27. Regad, J.: La torsion des trompes utérines, Gaz. d. hôp. **106**:557-562, 1933; Etude anatomo-pathologique de la torsion des trompes utérines, Gynéc. et obst. **27**:519-535, 1933.

28. Mosettig, E.: Zur Kasuistik isolierter Tubenstieldrehungen, Arch. f. Gynäk. **154**:421-431, 1933.

29. Rueder: Drei Fälle von Stieldrehung der Tube bei normalem virginellem Genitaltractus, Zentralbl. f. Gynäk. **45**:45, 1921.

In the same year (1933) Block and Michael [30] reported a case in a girl 13 years old, similar to the case we are reporting in this paper. In reviewing the literature they do not mention two cases reported by the Italian author Caucci [31] in 1932. Caucci reported six of his own cases. Two of them were cases of isolated torsion of the tube in two virgins, both 19 years old.

In comparing all these reviews we notice considerable divergence in the statements concerning the occurrence of the reported condition. The terms used in describing isolated torsion of the virginal or undiseased tube vary from "not infrequent" to "exceedingly rare." What are the reasons? This divergence may be partly due to an incomplete review of the literature. But it seems that the more important factor is the varying individual conception of the authors as to the "normality" of the twisted tube. If we were to analyze all reported cases with the necessary criticism, we should be forced to admit that a large number of reports lack the proof that the organ was undiseased before the torsion. In more than half of the reported cases a histologic examination is missing; many do not mention the condition of the ovary on the same side and of the adnexa on the opposite side; still others give an unsatisfactory past history from which a venereal infection cannot be excluded. In many cases it is difficult, even impossible, to decide whether or not the tube was normal before torsion. In the cases in which there is advanced necrosis of the wall even a most careful histologic examination may fail to detect mild inflammatory changes. The hemorrhagic infarction as the result of torsion and strangulation may hide to some degree the underlying pathologic process of the wall of the tube.

We recently had the opportunity to observe and study a case of isolated torsion of the fallopian tube in a girl 10½ years old. We report this case because of its rarity and in order to discuss the difficulties in deciding whether or not the organ was undiseased before torsion. And this even in a case where there is no doubt of existing virginity.

REPORT OF CASE

M. L., a white girl aged 10½ years, was referred to the Mount Sinai Hospital on Aug. 19, 1935, with a diagnosis of acute appendicitis. She gave a history of being seized with a severe pain in the right lower abdominal quadrant two days previous to hospitalization. It was the first time she had had such an attack. The pain was gradually subsiding. She was nauseated but did not vomit. Her previous history was irrelevant. She had had measles many years before the present illness and an attack of scarlet fever two months before. The scarlet fever

30. Block, F. B., and Michael, M. A.: Torsion of Normal Fallopian Tube, Am. J. Obst. & Gynec. **26**:268-270, 1933.

31. Caucci, A.: La torsione degli annessi uterine normali (sei osservazioni personali), Policlinico (sez. chir.) **39**:213-228, 1932.

was mild, and the rash subsided in twenty-four hours. The child made an uneventful recovery without any complications. There was no history of genital trouble or vaginal discharge, and the menses had not yet begun.

Physical examination revealed a fairly well developed and well nourished white girl 10 years of age, who appeared acutely ill. Her face was flushed. The temperature was 101.6 F., the pulse rate 132 and the respiratory rate 24. The abdomen was not rigid but was very tender to pressure in the right lower quadrant. The head, neck and chest were normal. Vaginal smears were done as a routine and showed no evidence of gonococci. Smears and cultures of material from the

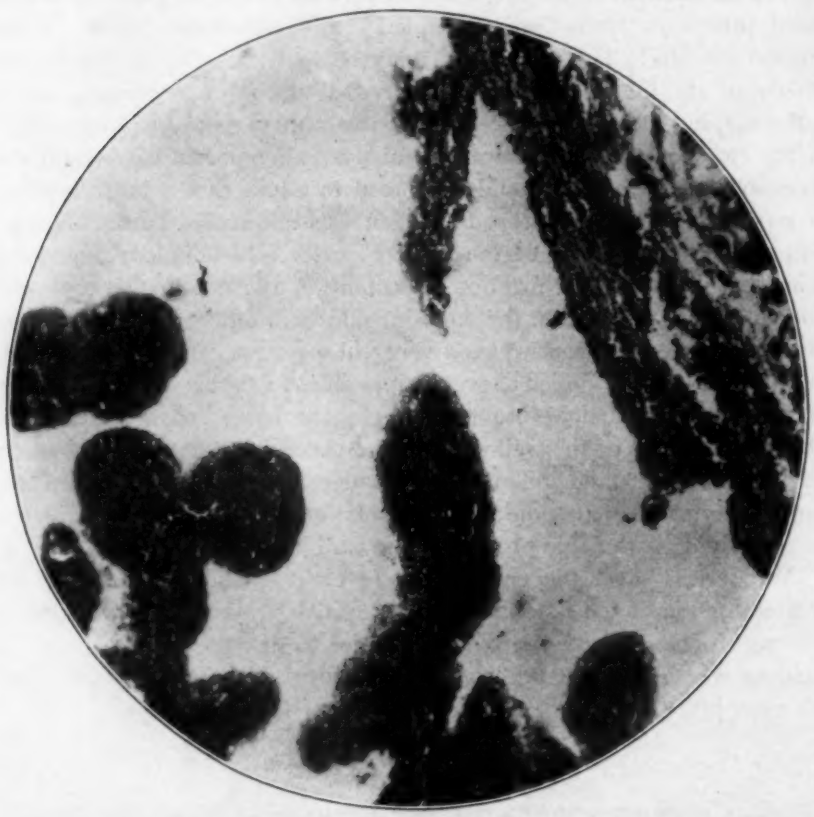

Fig. 1.—Low power photomicrograph showing hemorrhagic infarction of the tube. Note the diffuse hemorrhages extending into the folds. The epithelial lining is completely destroyed.

nose and throat were negative for Bacillus diphtheriae and hemolytic streptococci. The white cell count was 18,200, with 82 per cent polymorphonuclear leukocytes. The urine showed a faint trace of albumin. The diagnosis of acute appendicitis was confirmed, and the child was operated on immediately.

When the abdomen was opened through a muscle-splitting incision (Dr. B. Sayre), about 50 cc. of a blood-tinged fluid escaped. The appendix was injected and adherent to the omentum. Appendectomy was done, and the pelvis was

explored. In the hollow of the sacrum a large mass was palpable. This was finally brought up into the incision with some difficulty, and a black mass about the size of a large pear was revealed. The mass was followed down and found to be the right fallopian tube, which had twisted on itself in the clockwise direction with three complete turns. Its fimbriated end could not be demonstrated. The right ovary was in normal position and not involved in the torsion. It appeared slightly enlarged and had a few small cysts, which were punctured. The tube was untwisted and removed in the usual manner. Further exploration revealed an infantile uterus and a perfectly normal adnexa on the left side. The abdomen was closed without drainage, and the patient made an uneventful recovery, going home on the fifth postoperative day.

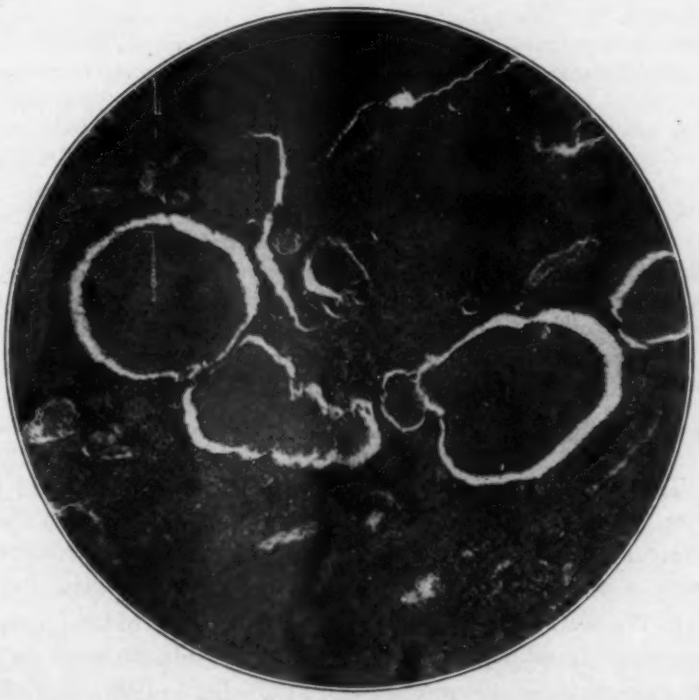

Fig. 2.—Low power photomicrograph showing hemorrhagic infarction of the tube. Part of the wall shows markedly distended capillaries and blood vessels with partly ruptured walls.

Pathologic Examination (Dr. I. Davidsohn and Dr. L. Blum).—Gross: The tube consisted of a cystic mass which measured about 85 by 42 by 13 mm. Its wall was a hemorrhagic membrane measuring from 1 to 2 mm. in thickness. The sectioned surface showed clotted blood, which was intimately connected with the wall and which could be separated from it only with considerable difficulty. No further morphologic details could be recognized grossly. The appendix measured 30 mm. in length and 17 mm. in the largest circumference. The serosa was markedly injected and showed evidences of adhesions. The lumen was patent and empty except for the tip, where it was occluded for a distance of 3 mm. The mucous membrane was somewhat edematous and showed occasional petechiae.

Microscopic Observations: Numerous sections from the wall of the cyst were prepared and studied. They showed essentially similar changes. The entire wall was full of extravasated blood. The veins and capillaries were maximally distended and filled with white and red blood cells. Some of them were thrombosed; others had ruptured walls. In places, there was present outside of the blood vessels a moderate number of lymphocytes and leukocytes. In a few sections hemorrhagic folds were present, resembling those of the mucosa of the fallopian tube. An epithelial lining was absent. Only occasional areas showed still preserved portions of the wall. The picture was that of a massive hemorrhagic infarction.

The mucosa of the appendix was somewhat hyperemic and contained a definitely increased number of eosinophilic leukocytes. A small number of them were also present in the submucosa and particularly in the muscularis. The serosa was markedly hyperemic and edematous and showed many perivascular accumulations of lymphocytes. This infiltration extended into the outer layers of the muscularis. The picture was that of chronic disproportionate periappendicitis.

A diagnosis of massive hemorrhagic infarction of the fallopian tube with resulting almost complete necrosis of the wall, and chronic periappendicitis (disproportionate) was made.

A few remarks concerning the results of the pathologic examination are necessary. After the first careful histologic examination of a considerable number of slides, no other changes, such as those of massive infarction, were found. But a few of the additional sections prepared in a special way for a more detailed study revealed occasional perivascular collections of round cells which were suggestive of a chronic inflammatory process. However, these perivascular infiltrations were made indistinct by the massive hemorrhagic areas.

COMMENT

This case presents the following particular features: (1) the occurrence of isolated torsion of the tube before puberty and the onset of menstruation, (2) a marked degree of the hemorrhagic infarction following torsion and (3) association with periappendicitis.

1. We were able to find in a careful search of the literature only three cases in which isolated torsion of the tube occurred in a girl not yet menstruating (Hansen,[20] 1922; Fiolle,[12] 1927, and Block and Michael,[30] 1933). Unfortunately, in Hansen's case a record of the histologic examination is missing, and from the description of Fiolle's case it is not clear whether the ovary was involved in the torsion. The case of Block and Michael presents several features similar to our own, which thus becomes the fourth on record. (For more details see the table). The lack of a connection with menstruation is an important point in considering the etiology and mechanism of such a torsion. In a large number of reports the evident connection of this accident with the venous congestion during menstruation is emphasized. Torsion occurred in many cases shortly before or at the time of menstruation. We will return to this point in discussing the etiologic factors.

2. The hemorrhagic infarction is a common result of torsion and strangulation, but advanced hemorrhagic necrosis and gangrene of the entire wall of the tube is much less common. We could not find any evident connection between the degree of torsion and the degree of the infarction resulting.

3. It is impossible to make a definite statement as to the frequency of coincidence of appendicitis and torsion of the tube. In most of the reported cases data on the histologic examination of the removed appendix are missing. A gross inspection alone is, however, fully unsatisfactory for determination of inflammatory changes in the appendix. The French authors Picot [32] and Ricard [33] reported two cases of torsion during acute appendicitis. Periappendical changes are more frequently observed at the operation. In our case the histologic picture was that of so-called disproportionate periappendicitis. Let us briefly stress the pathologic picture of this condition. The term "disproportionate periappendicitis" is applied to those inflammatory changes which affect the outer layers of the appendix in an acute or chronic manner—this in contrast to the noninvolvement of the mucosa, submucosa and muscularis. There are two different types of disproportionate periappendicitis: (1) periappendicitis following inflammatory changes within the pelvis, most frequently seen in women following salpingitis, and (2) periappendicitis following a subsiding, nonrecognized appendicitis. The latter type is common in children and is referred to as the juvenile type. It is possible to differentiate both types histologically. While in the first group the inflammatory changes are strictly limited to the serosa and the subserosa, in the juvenile type there is usually evidence of slight involvement of the inner layers. The results of the histologic examination in our case justifies its classification as the juvenile type of disproportionate periappendicitis.

With the findings of primary appendicitis or, strictly speaking, periappendicitis without appendicitis, the order of the intra-abdominal events may have been as follows: mild, nonrecognized appendicitis, subsiding appendicitis, disproportionate periappendicitis, mild perisalpingitis of the infundibular end of the fallopian tube, its closure, sactosalpinx, torsion and strangulation, infarction, hemorrhagic necrosis and free blood in the peritoneal cavity. We emphasize the word may because we cannot state with certainty that the mild periappendicitis had produced a localized perisalpingitis of the fimbriated end. The fundamental question arises:

32. Picot: Torsion de la trompe droite saine au cours d'une appendicite aiguë, Bull. et mém. Soc. nat. de chir. **58**:382-383, 1932.

33. Ricard, A.: Torsion de la trompe droite saine chez une jeune fille de quatorze ans. Appendicite aiguë concomitante, Bull. et mém. Soc. nat. de chir. **58**:1062-1066, 1932.

Was this case one of torsion of a normal fallopian tube in a virgin? The large balance of evidence favors the assumption of the integrity of the tube before torsion.

In favor of it are: (1) the age of the patient, (2) the occurrence before the onset of menstruation, (3) normal adnexa on the opposite side, (4) no history of vulvovaginitis in childhood and (5) mild acute exanthemas (measles and scarlet fever). Against it are: the findings of the closed fimbriated end and occasional accumulations of round cells on microscopic examination.

In the case reported we see how the overwhelming balance of evidence speaks for the integrity of the tube before torsion, and yet a definite determination is not possible, in spite of the careful histologic examination. We emphasize once again the importance as well as the difficulties of making the histologic examination. It is the most certain criterion for the integrity of the tube before torsion. Chastenet de Géry and Lacroix [34] reported a case of tubal torsion in a woman 29 years old. The tubes appeared perfectly normal on gross inspection, but only on microscopic examination were they found to be tuberculous.

In reviewing the literature we collected the reports of cases which appeared to us the most authentic ones of isolated torsion of the undiseased virginal tube and tabulated the data (see table). As to torsion of the doubtless pathologic virginal tubes, we refer to the cases collected by Anspach [3] and the case reported by Thorek.[14] Recently Askey [35] and Caucci [31] reported cases of torsion of pathologic tubes in virgins. Since we considered only torsion of the virginal tube, numerous cases reported during pregnancy are not included.

We do not intend to add to the existing definition of the "normal" tube another one, but we wish to make a few suggestions as to the points to be considered in giving an authentic report and in discussing torsion of the normal tube. The following points seem to us important:

1. Torsion should have occurred in a virginal genital tract in order to exclude all possibilities of venereal infection and the mechanical derangements following pregnancy.

2. In uncertain cases of virginity the age should be limited to the beginning of puberty (from 13 to 14 years).

3. The ovary and the adnexa on the opposite side should not show any gross pathologic process on operative inspection.

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34. Chastenet de Géry and Lacroix: Torsion des deux trompes en apparence normales et histologiquement tuberculeuses, Bull. et mém. Soc. nat. de chir. **53**: 558-561, 1927.

35. Askey, E. V.: Hydrosalpinx—with Torsion of Pedicle: Report of Case, California & West. Med. **37**:252-254, 1932.

4. A careful histologic examination must have been done. It should not reveal any evidence of inflammation, neoplasm or pregnancy.

5. In case of torsion on the right side the histologic examination of the removed appendix should not show periappendicitis to any marked degree.

In spite of our criticism of so many reports on torsion of the undiseased fallopian tube, we feel forced by the accumulated material to admit its possible occurrence. But the more precise reports would probably throw a little more light on the still obscure etiology and mechanism of this accident. There exists a rather extensive discussion in the literature on the etiology of torsion, and we refer the reader to these papers for more detailed information (Schweitzer,[9] Darner,[16] Gabe,[13] Koster,[17] Terruhn,[36] Saitz,[37] Shute [26] and others).

We present only briefly the advanced theories:

1. The hemodynamic theory. This theory, the oldest and most discussed one for explanation of torsion of intra-abdominal organs, was advanced by Payr.[38] It was applied by Schweitzer and other authors for an explanation of torsion of the normal fallopian tube. The essential fact in this theory is that the veins of the mesosalpinx are longer and more flexible than the arteries, and in cases of venous congestion they assume a spiral course, which favors torsion. In fact, it was possible to produce torsion artificially in such a manner. This theory is well fit to explain the numerous cases of torsion during pregnancy or in connection with menstruation. The literature reveals over twenty-five reports with an obvious connection of the torsion with the menses.

2. Sellheim's theory. Sellheim [39] advanced the theory of the transformation of the movements of the body on the internal organs. Sudden changes or stoppage of certain movements may produce torsion.

3. The anatomic theory. According to this theory, any malformation in the mesosalpinx or the anatomic structure of the tube favors torsion. The most frequent finding is an abnormally long mesosalpinx. Gengebach [40] found it in all of his six cases. Other factors also, such as acces-

36. Terruhn, E.: Zur Genese der Haematosalpinx unter der Berücksichtigung der Torsion, Ztschr. f. Geburtsh. u. Gynäk. **92**:432-449, 1927.

37. Saitz, O.: Zur Aetiologie der spontanen Tubentorsion, Zentralbl. f. Gynäk. **55**:222-224, 1931.

38. Payr, E.: Weitere experimentelle und klinische Beiträge zur Frage der Stieldrehung intraperitonealer Organe und Geschwülste, Deutsche Ztschr. f. Chir. **85**:392-451, 1906.

39. Sellheim, H.: Erklärung der Achsendrehung innerer Organe, sowie der Drehung, Umschlingung und Verknotung der Nabelschnur, München. med. Wchnschr. **69**:1237-1239, 1922.

40. Gengebach, A.: Sechs Fälle von Tubentorsion, Ztschr. f. Geburtsh. u. Gynäk. **97**:476-486, 1930.

sory ostia, hydatids of Morgagni, changes in the length and thickness of the tube and, last but not least, the persistence of spiral winding, may be of etiologic importance. Some postmortem observations on stillborn and new-born infants led us to believe that the persistence of the fetal tortuosity needs a more serious consideration in the etiology of the spontaneous torsion. Our observations correspond to those of Shute.

4. The physiologic theory. Recently, new physiologic factors were advanced for the explanation of torsion. It is a well known fact that the human tube as well as that of many animals undergoes varying physiologic contractions (Corner,[41] von Mickulicz-Radecki,[42] Mauclaire [43] and others). Disturbances of these regular peristaltic movements, such as spasm and other dysfunctions, are believed to be important etiologic factors (Darner [16] and Regad [27]).

5. The theory of the importance of a vulvovaginitis in childhood, genital complications of the acute exanthemas and attenuated tuberculosis. These factors have been emphasized by Anspach [3] and Norris [6] and recently by Thorek.[14] These diseases may have produced an unrecognized hydrosalpinx, thus creating a cystic structure. In contradiction to a general acceptance of this opinion, such as disease as gonorrhea, measles, scarlet fever or tuberculosis would probably have had a bilateral effect on the tubes, if any. Furthermore, in some reports we find the statement that the fimbriated end of the oviduct was open and the fimbriae were normal in appearance.

6. The traumatic theory. Five cases are reported in the literature in which the torsion followed an accident or trauma (Rueder,[29] Laemmle,[44] Koehler,[45] Cottalorda,[46] Charbonnier and Brandt [47]). If only *post hoc* and not *propter hoc*—we do not claim to decide it.

7. The theory of the influence of certain drugs. This factor must be considered. In the case reported by Caraven [11] torsion occurred after an application of apiol (parsley camphor; the dimethylmethylene ester of allyltetroxybenzene).

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41. Corner, G. W.: Cyclic Variation in Uterine and Tubal Contraction Waves. Am. J. Anat. **32**:345-351, 1923.

42. von Mikulicz-Radecki, F.: Zur Physiologie der Tube. Experimentelle Studien ueber die Spontanbewegungen der Kaninchentube in situ, Zentralbl. f. Gynäk. **49**:1655-1662, 1925.

43. Mauclaire: A propos de la torsion de la trompe utérine, Bull. et mém. Soc. nat. de chir. **53**:583, 1927.

44. Laemmle, K.: Ein weiterer Beitrag zur Frage der Eileiterdrehung, Zentralbl. f. Gynäk. **47**:436, 1923.

45. Koehler, M.: Torsion normaler Adnexe bei Enteroptose, Wien. klin. Wchnschr. **40**:1387-1388, 1927.

46. Cottalorda, J.: Torsion de la trompe saine en relation possible avec un traumatisme, Bull. Soc. d'obst. et de gynéc. **21**:551-553, 1932.

47. Charbonnier, A., and Brandt, H.: Un cas de torsion traumatique des annexes saines, Bull. et mém. Soc. nat. de chir. **61**:835-837, 1935.

As to the marked predominance of torsion on the right side, the following factors have been brought out to explain it: (*a*) the presence of the sigmoid colon on the left side, (*b*) the peristaltis of the small intestines on the right, (*c*) the spastic contractions of the cecum on the right and (*d*) the nearness of the appendix on the right.

If we try to apply any of the etiologic factors for an explanation of the case we are reporting, we shall find ourselves in difficulty. Torsion occurred before the onset of menstruation, there was no evidence of vulvovaginitis, the acute exanthemas were particularly mild, no abnormally long mesosalpinx was noted and no trauma occurred in connection with the torsion. In fact, the etiology in our case appears rather obscure and open only to pure theoretical speculations.

DIAGNOSIS

The acute forms of torsion are characterized by a sudden attack of severe pains in the iliac fossa, with rapid pulse and progressive agitation. The fever is mostly moderate and in no proportion to the rapidity of the pulse. This is considered an important differential diagnostic sign. The fever, leukocytosis and occasional presence of albuminuria result most probably from the absorption of toxins from the necrotic tube. Sometimes prodromal symptoms are present and are characterized by moderate pains in the iliac fossa during or at the time of menstruation. The established clinical picture is dominated by various functional disturbances. The pain is mostly marked. Muscular spasm is present in about 70 per cent of cases of torsion of the undiseased tube. Of the digestive troubles, vomiting is frequent (80 per cent), often being biliary in character. Later, an obstinate constipation frequently results. Urinary troubles, such as retention of urine and dysuria, are also rather frequent. Metrorrhagia is less common.

The frequency with which the symptoms of tubal torsion simulate a lesion of the appendix makes this mistake in diagnosis a frequent one. A careful rectal examination should be of value. The conditions involved in the differential diagnosis include, further: ovarian cyst with a twisted pedicle, rupture of a corpus luteum hematoma, biliary or renal colic, perforation of the intestine, intestinal obstruction, salpingitis and ectopic pregnancy.

Some of the French authors claim to have correctly diagnosed torsion of the tube clinically before operation. They have even described a syndrome of tubal torsion (Regad [27]). It is said to consist of the following signs: (1) a severe attack of pelvic pains, with agitation and anguish, appearing in the course of or in evident connection with menstruation; (2) rapid pulse coexisting with a nearly normal temperature; (3) the

presence of a palpable mass lateral to the uterus, of irregular consistency, mobile and extremely tender to touch, and (4) absence of any signs pathognomonic of tubal pregnancy.

In any case, torsion of the fallopian tube is now an established clinical and pathologic entity and must be thought of in all obscure abdominal accidents.

SUMMARY

A case of isolated torsion of the fallopian tube in a girl 10½ years old is reported, and the literature is reviewed.

Only three similar cases of tubal torsion in girls who have not yet menstruated have been reported previously. This case thus becomes the fourth on record.

A critical analysis of the reports on torsion of a normal tube reveals that many lack proof that the organ was undiseased before torsion.

The histologic examination is the most important criterion for the normality of the twisted tube. The difficulty of an exact determination whether or not the tube was undiseased before torsion is emphasized and illustrated in the reported case.

A sharp distinction is made between the tube of a virgin and that of a married woman. Reports of authentic cases of torsion of the normal virginal tube are collected from the world literature, and the data are tabulated.

Some suggestions are made as to how to determine authentic cases of torsion of normal tubes.

The etiology is briefly discussed, and the existing theories are presented. The etiology in the reported case is rather obscure.

EXPERIMENTAL STUDIES ON LYMPHATIC BLOCKAGE

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The fact that complete blockage of the lymphatic system has never been produced experimentally is testimony of the difficulty of causing such a condition. The explanation of this remarkable fact must lie in the capacity for the development of a collateral circulation. A multiple origin of the lymphatics from the veins was shown by Sabin.[1] She stated: "In the pig the lymphatics bud off from the veins in two places, from the anterior cardinal veins and from the veins of the Wolffian body. There are two sets of paired sacs, the jugular and the iliac; and two unpaired sacs, the retroperitoneal and the cisterna chyli." Later investigations by Clark and Clark [2] demonstrated that in the early stages of development of the chick there are numerous connections between the earliest lymphatics and the blood vessels. The complete picture concerning these anastomoses has not been determined, nor has it been established what proportion of these vessels remain capable of developing functional patency in adult life. Many investigators have found anastomoses between lymphatic vessels and veins, but the adequacy of the valves has made retrograde injection so difficult that such surveys are always incomplete.[3]

The maintenance of drainage through the thoracic duct has by many investigators been considered essential to life. Others have questioned the soundness of this theorem and have based their conclusions on

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Aided by a grant from the Division of Medical Sciences of the Rockefeller Foundation.

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Mrs. Gray's participation in this work was made possible by a grant from the Henry Strong Denison Research Foundation.

1. Sabin, Florence R.: The Origin and Development of the Lymphatic System, Baltimore, Johns Hopkins Press, 1913.

2. Clark, Eliot R., and Clark, Eleanor L.: Contrib. Embryol. **9**:449, 1920.

3. Job, T. T.: Am. J. Anat. **24**:467, 1918.

numerous experiments in which the duct itself has been blocked or obliterated. On the other hand, these arguments are obviously worthless, since it has been demonstrated that there is a widespread network of anastomosing vessels between the lymphatics and the veins, and hence negative experiments are meaningless. Not only has this condition made impossible the determination of the extent to which the lymphatic system is essential to the life of the organism, but it has rendered difficult the analysis of the physiologic significance of the system in part and as a whole. Furthermore, in regard to localized areas, the enormous regenerative capacity possessed by lymphatics (Reichert [4]) has made an analysis of their local importance extraordinarily difficult.

In approaching the study of lymphatic drainage and in planning experiments for the elimination of this drainage, the principal objectives were to answer these queries: 1. Is the integrity of the lymphatic system necessary to life? 2. What effect does elimination or blockage of the lymphatic system have on the supply of leukocytes to the circulating blood? 3. What effect does this blockage have on the nutrition of the animal and, in particular, on the absorption and utilization of fats? The present series of experiments has been projected in an effort to answer these three questions. Information has been obtained which illuminates them to some extent, but much more elaborate studies will be necessary before a final answer can be obtained concerning the basic physiology of the lymphatic system.

In considering the first of these questions, it may be stated that no definite proof is available from previous studies as to whether or not the integrity of the lymphatic system is essential to life. This is due simply to the fact that there has never been any certain demonstration of complete blockage. It is known that man and experimental animals tolerate occlusion of the thoracic duct. On the other hand, a fistula of the thoracic duct is usually associated with a loss in weight and death.

In considering the alterations in the cellular picture of the blood, it is important to consider the observations of Lee.[5] After ligation of the thoracic duct in the chest, an immediate decrease in the lymphocytes to 56 per cent of the original level was noted, the count returning to normal in the third week. This return to normal was believed by Lee to result from the establishment of a collateral lymphatic circulation.

The present situation as regards the studies on the cellular composition of the blood after obstruction of the lymphatics is summarized by Drinker and Field [6] as follows: "No experiments are available in

4. Reichert, Frederick Leet: The Regeneration of the Lymphatics, Arch. Surg. **13**:871 (Dec.) 1926.

5. Lee, Ferdinand C.: J. Exper. Med. **36**:247, 1922.

6. Drinker, Cecil K., and Field, Madeleine E.: Lymphatics, Lymph and Tissue Fluid, Baltimore, Williams & Wilkins Company, 1933.

which all the lymphatic entrances on the left and right sides have been either ligated or exteriorized, and without such experiments we can have but an idea of the effects of lymph blockage on the cellular composition of the blood." The literature on the cellular composition of the lymph from the thoracic duct has been reviewed by Drinker and Field and need not be repeated here in detail. After a consideration of the studies of the lymph from the thoracic duct, as well as of the experiments of Lee, it is obvious that the inflow of lymph into the vascular system from the thoracic duct must be of considerable importance in determining the relative percentages of lymphocytes present in the circulating blood.

The third point of interest in relation to blockage of the lymphatics has to do with the possibility of producing nutritional disturbances by preventing the entrance of fat into the blood stream. The fact that lymph may enter the subclavian veins through the right lymphatic duct has not been taken into consideration in most of the work. Drinker and Field stated: "The problem of nutritional disturbances and survival after excluding the lymph from the circulation seems never to have been attacked with much success, not because the thoracic duct has not been tied but because failure to tie the entrances on the right side or else the onset of infection have vitiated the results." Bloor [7] stated that 60 per cent of the absorbed fat is the largest amount that has been recovered from the thoracic duct. Perhaps the most significant work on the relationship of lymphatic obstruction and nutritional disturbances is that of Schmidt-Mülheim.[8] He divided the left lymphatic, or thoracic, duct and the right lymphatic duct and ligated the veins in the lower part of the neck into which the ducts enter. No nutritional disturbances were observed in the animals, and he found that the lymphatic apparatus was not necessary for the passage of the products of protein digestion into the blood stream. Lee [9] found no evidence of nutritional disturbances in cats which were observed for as long as seventy-seven days after the occlusion of the thoracic duct. In summary, the evidence to date indicates that patency of the thoracic duct is not essential. However, attempts to block the entrance of lymph into the circulation have not been successful.

Our interest in the present problem was aroused by the results of experiments [10] on dogs and cats in which the superior vena cava was ligated. Chylothorax resulted from this procedure in approximately 50 per cent of the animals. It seems likely that the accumulation of chyle

7. Bloor, W. R.: Physiol. Rev. **2**:92, 1922.

8. Schmidt-Mülheim, Adolf: Arch. f. Anat. u. Physiol. (Physiol. Abt.), 1877, p. 549.

9. Lee, Ferdinand C.: Bull. Johns Hopkins Hosp. **33**:21, 1922.

10. Blalock, Alfred; Cunningham, R. S., and Robinson, C. S.: Ann. Surg. **104**:359 (Sept.) 1936.

in the chest after ligation of the superior vena cava is due to interference with the normal emptying of the lymphatic ducts into the tributaries of this vein as a result of the high venous pressure. Most of the animals remained in good condition if the chyle was aspirated frequently from the chest in order to prevent too great a reduction in the vital capacity. After varying intervals of time, the reaccumulation of chyle in the pleural cavities ceased. This was thought to bear a relationship to the decline in venous pressure as the collateral veins increased in size. An analysis of the condition which ensued after occlusion of the superior vena cava was complicated by the fact that one could not separate with certainty the effects of venous obstruction alone from those effects due to the impediment to the flow of lymph. Since occlusion of the superior vena cava cannot be produced without causing an increase in the pressure in the lymphatics which drain into it, it was decided that an attempt should be made to block the lymphatics themselves without causing an associated venous obstruction. It was with this idea in mind that the experiments reported here were begun. They have been extended to include studies on the cellular composition of the blood before and after occlusion of various lymphatic vessels. In addition, the state of nutrition of the animals has been observed, and an attempt has been made to determine whether or not patency of the lymphatic system is essential to life. A few studies, as yet incomplete, have been performed in which the fat in the blood was determined repeatedly after the feeding of cream by stomach tube.

METHODS

Dogs were used as the experimental animals in some instances and cats in others. All of the operations were performed with the animal under general anesthesia, inhalation ether being used in some experiments and pentobarbital sodium, administered intravenously, being employed in others. Various operative procedures were carried out in the attempts to produce complete blockage of the lymphatic system. A total of two hundred and sixty-seven operations were performed on fifty-two dogs and twenty-two cats, or an average of almost four operations per animal. The greatest number of operations on a single subject was seven. The operative procedures were not spaced at regular intervals. It was believed at the beginning of the work that the greatest likelihood of producing lymphatic obstruction would be found in chronic experiments in which infrequent operations were performed and in which the animals were observed for long periods. Later, when it became evident that this procedure had failed to produce obstruction, it was decided that the best possibility rested in the causing of massive obstruction of the lymphatic system without allowing sufficient time for the development of large collateral lymph vessels. The order of the operative procedures also varied in the different experiments. In some instances the initial operative attack was on the large ducts at the entrances into the veins of the neck. In other experiments attempts were made first to block the lymphatics nearer the points of origin and subsequently to occlude the lymphatic ducts.

A brief description of the various operative procedures follows. These procedures include: 1. Ligation and division of the thoracic duct in the neck. An

incision was made over the left external jugular vein in the lower third of the neck, and the tissues were freed from the proximal portion of the vein. The danger of entering the pleural cavity was minimized by adhering closely to the wall of the vein in the dissection. The thoracic duct could be found without difficulty, and it was doubly ligated and divided. In addition, any other ducts which were seen were ligated. 2. Ligation and division of the lymphatic duct on the right side of the neck. The duct was exposed in much the same way as the thoracic duct. An incision was made over the proximal part of the external jugular vein, and the junction of the jugular and the axillary vein was exposed. Usually, the lymph vessels could be seen; and when noted they were ligated and divided. 3. Intrathoracic occlusion of the thoracic duct. This operation is an extension of that described by Lee.[9] An intercostal transpleural incision was made at the level of the eighth thoracic vertebra. The surrounding tissues were separated from the wall of the aorta. These tissues, together with the thoracic duct and the azygos vein, were doubly ligated. Sodium morrhuate was injected into them. In addition, the mediastinal pleura, separating the two pleural cavities, was tied doubly and divided at a level slightly below the apex of the heart. 4. Ligation and injection of the cisterna chyli. The cisterna was usually exposed through an incision in the left flank, although an approach on the right was used in a few experiments. The cisterna was visualized as it lies just posterior to the abdominal aorta. Sodium morrhuate was injected into the cisterna, and it was dissected away from the aorta as completely as possible. An attempt was made to ligate some of the lymphatics which entered the cisterna. Several cubic centimeters of sodium morrhuate was left at the site from which the cisterna had been removed. 5. Attacks on the lymphatics and lymph nodes in the peritoneal cavity. These procedures were numerous and varied. In some experiments all of these were carried out, while in others only one or more were used. One of these procedures consisted of the injection of sodium morrhuate (Searle) or quinine and urea hydrochloride (usually the former) into the mesenteric lymphatics. A small needle was introduced into these lymphatics a short distance from the wall of the intestine, and the solution was injected. As many of the mesenteric lymphatics as possible were treated in this manner. In some experiments the injection of the sclerosing solution was followed by the introduction of crystalline silica (Drinker). Another procedure consisted of the injection of one of the sclerosing solutions into the larger lymph vessels which lie just behind the posterior peritoneum and to either side of the vertebral column. These vessels were quite prominent in the animals in which the large trunks in the chest had been occluded. This was particularly true of the lymph vessels in the neighborhood of the junction of the renal veins and the inferior vena cava. In some instances a number of these lymph vessels were ligated. Still another procedure consisted of the injection of sclerosing solutions directly into the lymph nodes. A needle was inserted into the substance of the various glands, and the solution was introduced slowly.

As has been stated, the order of the operations varied in the different experiments. In a few of these as many as three of the procedures were performed on the same day. This was done with the idea of producing as massive an obstruction as possible. The quantity of the sclerosing solutions which can be injected without causing death was the limiting factor in the extent of the procedures that were carried out in the peritoneal cavity. It was found not to be safe to introduce more than 15 cc. of the sodium morrhuate at one operation into a dog weighing 10 Kg.

In the majority of the animals studied, blood counts were made several days preceding the first operation and were continued for periods varying from a few weeks to several months, usually at biweekly or triweekly intervals. Total white blood cell counts were made in the usual manner. The differential counts were done on coverslip preparations stained with Wright's stain. At the time the blood was taken several pairs of coverslips were pulled, and the best pair was selected; both coverslips were stained, and 200 or 400 cells were counted on each. As was pointed out by Sabin, Cunningham, Doan and Kindwall,[11] more accurate results are obtained by this method than by counting the same number of cells on a single coverslip. It has been our routine to count 200 cells on each coverslip when the total counts were under 20,000, and 400 cells when they were above 20,000. The technical difficulties involved in studying so large a series of animals with the supravital method made its use in these experiments impossible. While qualitative changes undoubtedly must exist in these cells, our objective at the moment was to utilize the blood more as a control for the effect of the operative procedures than to examine any qualitative effects of the operative procedures on the cells of the blood. This will, however, be taken into consideration in further experiments.

The superior vena cava was ligated in a few of the experiments. This was usually done toward the end of the observation period and when the effects of the lymphatic blockage, as reflected in the cellular picture of the blood, had disappeared.

As has been stated, the cellular composition of the blood was determined frequently in most of the experiments, and the animals were observed for varying intervals of time. In some instances the period of observation was terminated by the spontaneous death of the animals; in others, death was caused painlessly when the appearance of the animal and the cellular picture of the blood indicated that death was imminent. In still others (and these constituted the majority of the experiments) the animals were killed while still in good condition, and careful autopsies were performed. The autopsies included a careful search for lymphaticovenous communications. This search was carried out most successfully by bleeding the animals almost to the point of death and then washing out the greater part of the remaining blood by the introduction of salt solution under pressure into the circulation. Immediately after death, a solution of berlin blue was injected into the lymphatics, and a search was made for communications between the lymphatics and the veins. The removal of the red blood cells greatly facilitated the search.

RESULTS

Fifty-two dogs and twenty-two cats were used in these studies. A variety of operations have been performed, but, in general, these have consisted of blocking the lymphatic ducts in the neck and chest, of destroying the cisterna and of interfering with the drainage of the mesenteric lymphatics. The animals were studied over periods ranging from a few days to several months; hence complete uniformity of results was not obtained. In many of the animals there was undoubtedly temporary obstruction, which was relieved by the opening of the

11. Sabin, F. R.; Cunningham, R. S.; Doan, C. A., and Kindwall, J. A.: Bull. Johns Hopkins Hosp. **37**:14, 1925.

collateral lymph channels, and in these animals there was a marked temporary change in the blood picture, with a return to normal. There were many examples of this sort. For example, in dog 34 there was obviously marked obstruction after ligation of the ducts and destruction of the cisterna. The lymphocyte count fell from 2,318 to 787 cells and the eosinophil count, from 688 to 164. At autopsy, however, communications with the inferior vena cava were demonstrated, and prior to autopsy the number of both the lymphocytes and the eosinophils had

TABLE 1.—*Data on Animals with Complete Obstruction*

Dog No.	Group No. (table 5)	Comment
15	I	Mesenteric lymphatics appeared as large white cords; no L-V* communications
28	I	All lymphatics in abdominal viscera tremendously dilated with chyle; no L-V communications
121	VII	Mesenteric lymphatics appeared as large white cords in many areas; no L-V communications

* Lymphaticovenous.

TABLE 2.—*Data on Animals with Marked Obstruction*

Dog No.	Group No. (table 5)	Comment
2	VII	Chyle extravasated into mesentery; mesenteric lymphatics dilated; lymph nodes enlarged; no L-V* communications
3	I	Marked distention of lower abdominal lymphatics; no L-V communications
13	III	Marked obstruction of mesenteric lymphatics; no L-V communications
41	II	Generalized retrograde injections; small amount of extravasated chyle in mesentery; small duodenal ulcer; no L-V communications
108	VII	Mesenteric lymphatics appeared as large white cords; generalized retrograde injection; no L-V communications
114	II	Marked obstruction of mesenteric lymphatics (ileum); no L-V communications

* Lymphaticovenous.

increased, although the averages had not returned to the preoperative level.

Before the alterations in the cellular composition of the blood were considered, the data in regard to lymphaticovenous communications as shown at autopsy will be enumerated. In nine experiments a careful search did not reveal such connections. The obstruction was complete in three of these, and the data are enumerated in table 1. These experiments will be described in detail. There was evidence of marked blockage in the remaining six experiments, and the data are contained in table 2. There were eleven animals which showed partial obstruction and in which communications were demonstrated with veins other than the normal connections which had been destroyed at operation. In most

instances these connections included anastomoses with the vena cava. In some of these animals temporary blockage occurred, but in none of them was the blockage maintained to a fatal termination or to an extensive degree. The data are enumerated in table 3.

In the study of the cellular picture of the blood the lymphocytes were looked on as the principal indication of changes in the blood cells; changes in other cells have been, as far as possible, related to changes in the lymphocytes. This method of approach was taken because it has been shown by many observers that there are large numbers of lymphocytes in the lymph from the thoracic duct. Rous [12] found that these cells

TABLE 3.—*Data on Animals with Partial Obstruction*

Dog No.	Group No. (table 5)	Comment
7	VII	Dilated lymphatics in anterior mediastinum, over surface of pericardium and on surface of large intestine; L-V* communications with inferior vena cava
14	I	Plexus of distended vessels under trachea; L-V communications with axillary vein
17	IV	Regional obstruction of intestinal lymphatics; lymphatics of omentum prominent; L-V communications with inferior vena cava
22	I	Regional obstruction of intestinal lymphatics; L-V communications with inferior vena cava
23	IV	Regional obstruction of mesenteric lymphatics; L-V communications with inferior vena cava and lumbar vein
29	II	Duodenal lymphatics prominent; L-V collaterals possibly above diaphragm
30	I	Regional mesenteric blockage; L-V communications with inferior vena cava and lumbar vein
44	V	Regional mesenteric blockage; L-V communications with inferior vena cava and mesenteric vein
46	VI	Regional blockage of intestinal lymphatics; L-V communications with vena cava and lumbar vein
72	VII	Generalized retrograde injection; L-V communications questionable
101	VII	Lymph nodes seminecrotic; some clotted material in lymphatics

* Lymphaticovenous.

constituted from 69.8 to 96.8 per cent of the total number of white cells, with an average of 87.6 per cent. According to counts of Bunting and Huston,[13] there are more lymphocytes poured into the circulation in twenty-four hours than there are total numbers of lymphocytes in the circulating blood at any time.

In general, the plan of approach was to take several preoperative counts, to determine the general level of cells in these animals and then to follow them at regular intervals, usually two or three times a week thereafter. Such a procedure made possible the determining of a continuous curve from the beginning of the experiment to its cessation. Some of these lasted only a few days, and others, several months. To

12. Rous, F. Peyton: J. Exper. Med. **10**:537, 1908.
13. Bunting, C. H., and Huston, John: J. Exper. Med. **33**:593, 1921.

analyze these experiments with any degree of objective value has been difficult, since recovery by the development of collateral circulation has been the rule, and hence the evaluation of each operation has been necessarily a part of the curve.

We have attempted to analyze all of the experiments done in terms of changes in the blood, regardless of whether or not permanent blockage occurred, as we felt it important to discover the effect of temporary as well as permanent blockage on the cells of the blood. A brief summary of the results is given in table 4.

The total number of dogs for which blood counts were made was forty-four. These animals have been arranged in seven groups, as shown in table 5. Groups I and II, as will be noted, differ only in that the dogs in group II showed no change in monocytes, while those in group I showed

TABLE 4.—*Summary of Blood Studies in Dogs*

Changes in Blood Picture	No. of Dogs Studied		
	With Preliminary Counts	Without Preliminary Counts*	Total
1. Decrease in lymphocytes	23	6	29
2. Decrease in lymphocytes and eosinophils	20	4	24
3. Decrease in lymphocytes and eosinophils with an increase in monocytes	12	3	15
4. Decrease in eosinophils only	3	0	3
5. Increase in monocytes only	2	2	4
6. No change in blood picture	5	3	8
Total number of dogs studied			44

* Since no preliminary counts were made, the averages for normal dogs were used for comparison.

a marked increase. Group VII consists primarily of animals on which no preliminary counts were made; therefore, we could not be certain of an increase or decrease in the cell count after the first operation. Nevertheless, in comparison with the average level in normal animals, it is perfectly obvious that certain of these, such as dog 121, had partial or complete blockage after the operation and hence could be included in the group of animals showing a decrease in lymphocytes and eosinophils. Calculated in this way, it will be noted that twenty-four animals showed a consistent decrease in eosinophils and lymphocytes, and five additional animals (a total of twenty-nine) showed a consistent decrease in lymphocytes alone. While this is not in any sense final proof of a profound association between these two types of cells, it is nevertheless extremely sound evidence that there is some effect on the eosinophils of the circulation after obstruction to the inflow of lymph into the blood stream. In eight of the animals there was no change in the blood picture, and in fifteen animals there was no appreciable decrease in

lymphocytes after any of the operations. These negative results are obviously explicable in terms of an immediately available collateral circulation. With the tremendous development which the collateral circulation is capable of undergoing, it is perfectly obvious that we cannot assume that a failure to obtain a decrease in lymphocytes after ligation of the thoracic duct in any way invalidates the theory of the importance of the lymph supply to the maintenance of lymphocytic inflow into the circulation. Assuming these facts to be true, the experiments carried out here demonstrate, first, that in a large proportion of the animals there is definite evidence of lymphatic blockage in terms of reduced supply of lymphocytes to the circulating blood after obstruction and that in the majority of these animals there is a corresponding diminution in the supply of the eosinophils. An important but less marked change is the increase in the monocytes, which, while present in a considerable number of animals (nineteen,), does not seem to be of quite the same importance as the change in lymphocytes and eosinophils. Nevertheless, since this increase in monocytes occurred in fifteen of the twenty-four animals which showed changes in lymphocytes and eosinophils and in only four animals in which these changes did not occur, it would suggest a possible relationship to be investigated further. The three animals which were considered to have complete blockage (table 5) showed a marked decrease in the lymphocytes and eosinophils, and two of them showed a marked increase in the monocytes.

The results of three experiments in which the evidence for lymphatic blockage was most striking will be described in detail.

Dog 28.—The first operation on dog 28 was performed on May 13, 1935. It consisted of exposing the thoracic duct through a transpleural incision at the level of the eighth dorsal vertebra. It was doubly ligated together with the azygos vein and the tissues surrounding the aorta. Sodium morrhuate was injected into the structures both above and below the ligatures. In addition, the mediastinal pleura and the cardiac ligament were doubly ligated and divided. The incision into the chest was then closed. This procedure was performed under positive pressure intratracheal anesthesia. The second operation was performed on May 24; in fact, three operations were performed on this date. Incisions were made on the right and left sides of the neck, and the lymphatic ducts were ligated and divided. An incision was then made in the left flank, and the cisterna chyli was exposed. The cisterna was filled with solid material which looked like chyle that had clotted. The greater part of the cisterna was removed. Several cubic centimeters of sodium morrhuate was placed in the neighborhood of the aorta, and the incision was closed.

The animal seemed to get along satisfactorily for the following five days, but became quite short of breath on the sixth day, May 30. Both pleural cavities were aspirated at this time, 600 cc. of fluid being obtained from the left side and 250 cc. from the right. The fluid was whitish yellow. After it had stood, a sediment which equaled approximately one fourth of the total volume precipitated out. When shaken, the fluid was flaky. This fluid showed a total count of

120,000 cells per cubic millimeter. Supravital studies showed that these cells were all polymorphonuclear leukocytes, with the exception of an occasional clasmatocyte. They were all living cells, but practically every cell contained a peripheral ring of fat droplets.

The following day, May 31, the animal appeared ill, and it was decided to kill him, since death would have occurred almost certainly within twenty-four hours. The respiratory rate was rapid. The eosinophils had disappeared from the blood

TABLE 5.—*Blood Changes in Dogs Selected as Typical of Each Group*

Group*	Lymphocytes	Eosinophils	Monocytes
Group I (12 animals)			
Dog 15†			
Preliminary (5)‡	3,088	3,148	699
1. Duct (11)	384	191	2,318
Dog 28†			
Preliminary (3)	1,441	929	877
1. Thoracic (5)	1,362	223	2,686
2. Duct and cisterna (2)	500	0	2,022
Group II (7 animals)			
Dog 41#			
Preliminary (4)	1,991	1,299	919
1, cava; 2, lymph nodes; 3 cisterna (2)	240	22	934
Dog 49			
Preliminary (3)	2,020	2,010	1,050
1. Thoracic (15)	561	302	1,191
Recovery (10)	1,583	4,100	1,570
Dog 114#			
Preliminary (1)	1,824	432	2,688
1. Removal of spleen (1)	584	365	1,314
2. Thoracic (5)	467	342	2,378
Group III (3 animals)			
Dog 107			
Preliminary (1)	1,572	736	2,024
1. Abdominal (2)	400	606	1,085
2. Chest (5)	343	239	1,905
3. Abdominal (7)	565	260	1,838
Group IV (3 animals)			
Dog 47			
Preliminary (3)	1,766	2,811	354
1. Thoracic (5)	1,496	608	1,559
2. Duct and cisterna (6)	1,182	1,005	1,959
Recovery (5)	1,280	1,552	709
3. Abdominal (5)	738	632	982
Group V (2 animals)			
Dog 104			
Preliminary (1)	400	200	800
1. Cisterna (6)	642	200	1,465
Recovery (12)	2,287	730	1,131
2. Duct (12)	1,629	512	1,049
Group VI (7 animals)			
Dog 46			
Preliminary (3)	2,040	1,107	2,467
1. Thoracic (6)	2,467	993	3,674
Recovery (15)	1,887	1,136	1,778
2. Duct and cisterna (7)	1,354	1,207	2,273
Group VII (9 animals)			
Dog 108#			
2 previous operations			
Preliminary (3)	416	99	1,659
3. Abdominal (1)	390	0	2,496
Dog 121‡			
3 previous operations			
Preliminary (3)	883	497	1,777
4. Abdominal (11)	388	114	1,125
5. Thoracic (3)	262	105	1,888

* The dogs were divided as follows: group I, dogs in which there was a consistent decrease in eosinophils and lymphocytes with an accompanying increase in monocytes; group II, dogs in which there was a consistent decrease in lymphocytes and eosinophils, but with no accompanying change in monocytes; group III, dogs in which there was a decrease in lymphocytes with no consistent change in other cells; group IV, dogs in which there was a decrease in eosinophils with no consistent change in other cells; group V, dogs in which there was an increase in monocytes with no consistent change in other cells; group VI, dogs in which there were no marked changes in the leukocytes, and group VII, miscellaneous.

† This animal showed complete obstruction at autopsy.

‡ This and other numerals in parentheses represent the number of blood counts made, and the counts given are averages of these.

This animal showed marked obstruction at autopsy.

stream, and the lymphocytes were greatly reduced in number. When the peritoneal cavity was opened, the walls of the stomach and of the entire intestinal tract down to the descending colon were observed to be tremendously infiltrated with chyle. This infiltration started in the base of the mesentery and progressed outward to a considerable distance as an almost solid mass of chyle. There were enormous numbers of lymphatics which obviously had ruptured, but there were also many discrete vessels, particularly over the intestinal wall; these vessels were seen to empty into the mass of extravasated chyle (fig. 1*A*). All lymph nodes were enormously enlarged, and fluid exuded from their surfaces. The lymph vessels leading from the pelvis were either ruptured or so greatly distended that

their walls could not be made out. The omentum showed an extraordinary injection of the lymphatics in which parallel vessels followed each band of fatty tissue throughout the network of the structure. This is shown to some extent in figure 1*B*, but the photograph does not reveal the true degree of the engorgement of these lymphatics. The lymphatics of the gallbladder, pancreas and hepatic pedicle were enormously dilated. Approximately 10 cc. of yellowish, milky fluid was removed from the peritoneal cavity. The enormous distention of the lymphatics is shown in figures 2*A* and *B*, sections taken from the pancreas and omentum, respectively. In figure 2*C* the distended lymphatics of the submucosa and muscular layers of the intestines are shown containing coagulated lymph.

The chest was opened, and 550 cc. of fluid was removed from the right pleural cavity and only a small quantity from the left. The fluid looked like milk to which had been added a slightly yellowish pigment. The pericardial cavity contained 30 cc. of pure white fluid. The anterior mediastinal lymph nodes and tissues were completely infiltrated with this same fluid. Slight pressure caused obvious leakage, and it appeared that it was through this area that fluid obtained egress into the pleural cavities. Block dissection was used, and the tissues were removed from the neck to the lower portion of the colon. These were fixed immediately in a solution of formaldehyde. The posterior wall of the abdomen was examined, and two large lymph nodes were observed on either side of the vertebral column at the level of the sacral crest; these nodes were approximately 3.5 by 2.5 cm. in size.

In figure 3 and table 5 the counts on the peripheral blood of dog 28 are presented. It will be noted that there is a marked decrease in the eosinophils after the first operation but none in the lymphocytes until after the ligation of the lymphatic ducts. The animal became extremely weak and was killed before the lymphocytes had had sufficient time to reach a stabilized count. The eosinophils had disappeared from the blood stream, and the level had been extremely low for four counts previous to their disappearance. There was a marked increase in the total count, which was explained by the increase in neutrophils which accompanied it. The monocytes were definitely but irregularly increased after the first operation and maintained this high level throughout the course of the experiment.

Dog 15.—This animal weighed 11.75 Kg. After preliminary studies of the cellular picture of the blood, operations were performed on March 7, 1935. Incisions were made on both sides of the neck, and the large lymphatic ducts were ligated and divided. An incision was made in the left flank, and the cisterna chyli was exposed. It was distended with fluid. The major portion of the cisterna was dissected away from the aorta and removed. Several cubic centimeters of sodium morrhuate was placed in the neighborhood of the aorta, and the incision was closed.

Twelve days after the operation, 920 cc. of whitish, slightly blood-tinged fluid was aspirated from the chest. The following day 405 cc. of white fluid was removed. On March 21, two weeks after the operation, the weight had declined to 10.25 Kg. During the succeeding four days a total of 785 cc. of fluid that looked like milk was aspirated from the chest. On March 26 the weight of the dog had decreased to 9 Kg., and three days later it was 7.65 Kg. On the latter date the dog had diarrhea. One hundred cubic centimeters of fluid was withdrawn from the chest at that time. On March 30 and April 1 125 cc. of milky, slightly yellowish fluid was removed. The animal appeared to be quite weak on the latter date. No food had been taken for several days, and the animal had ceased to walk around. When seen at 8 o'clock in the evening of April 1, it seemed doubtful if the dog would survive until the following morning. The temperature was 98.8 F., and the

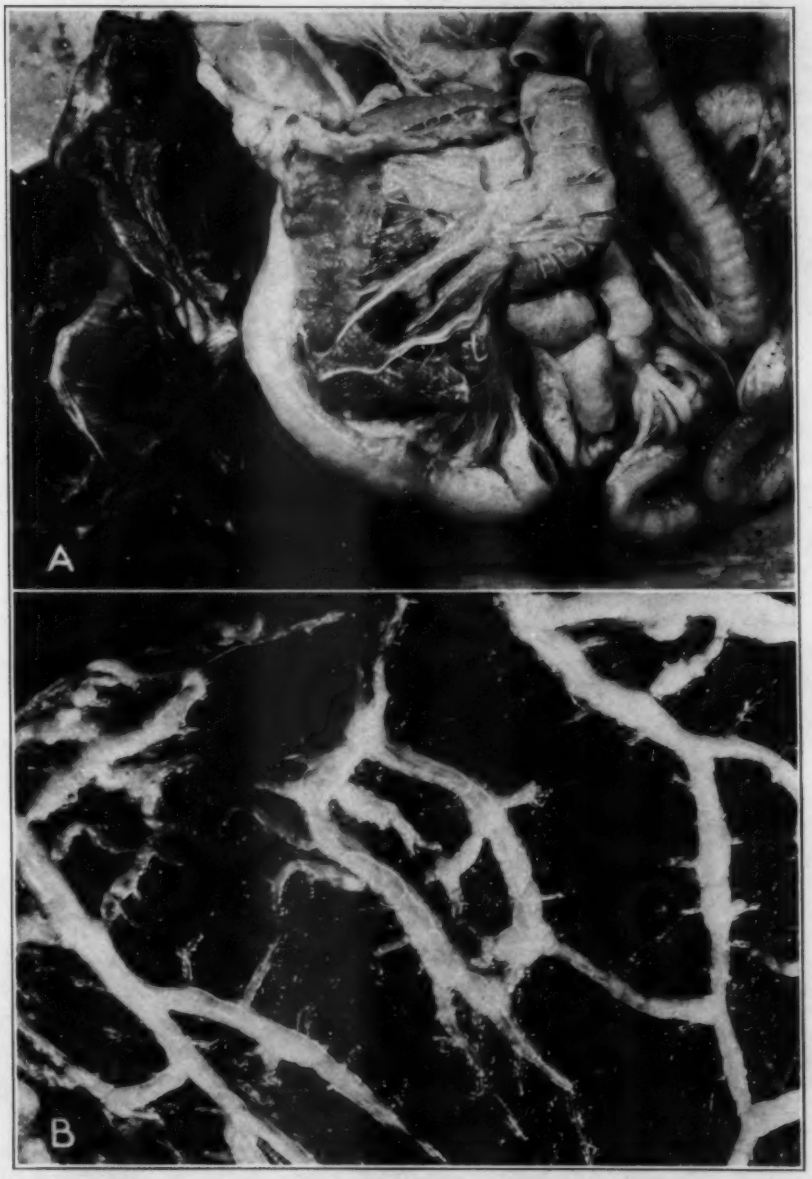

Fig. 1.—*A*, photograph of the duodenum and pancreas of dog 28, showing enormous numbers of lymphatics in each of these structures. *B*, photograph of the omentum of dog 28. The lymphatics are loaded with fat and can be seen as small thin white lines in the fatty areas.

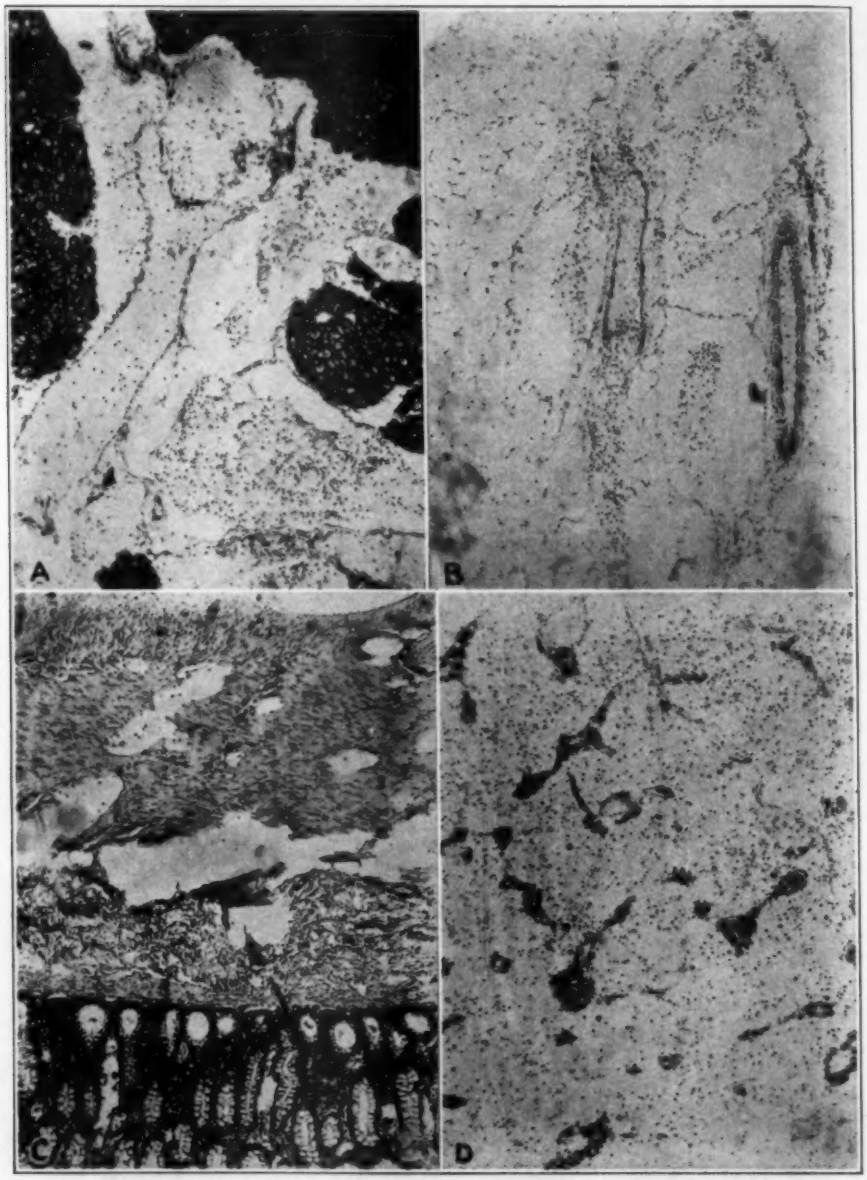

Fig. 2.—*A*, photomicrograph of a section of the pancreas of dog 28, showing enormous distention of the perivascular lymph vessels; × 50. *B*, photomicrograph of a section of the omentum of dog 28, showing marked distention of the lymphatics; × 50. *C*, photomicrograph of a section of the large intestine of dog 28, showing a marked dilatation of the lymphatics in the submucosa and muscularis; × 50. *D*, photomicrograph of a section of the lymph node of dog 15, showing marked dilatation of the central sinus system. The lymphoid tissue is thinned out, depressed and somewhat decreased in amount; × 50.

pulse had a rate of only 98 per minute but was weak. The respiratory rate was not rapid, and the weight was 6.97 Kg. Ether was given by cone, and an abdominal incision was made. The animal died after only a small amount of ether had been administered.

Autopsy showed that most of the mesenteric lymph vessels leading from the small intestine were large white cords which were filled with solid material (fig. 4*A*). In the mesentery of the lower part of the ileum several lymphatics were observed which did not contain coagulated material. Berlin blue was injected into these, but the solution did not pass beyond the adjacent lymph node. The lymph nodes were large and edematous. The pleural cavities contained a total of 135 cc. of milky, slightly yellowish fluid. There was no pneumonia. The thoracic duct was

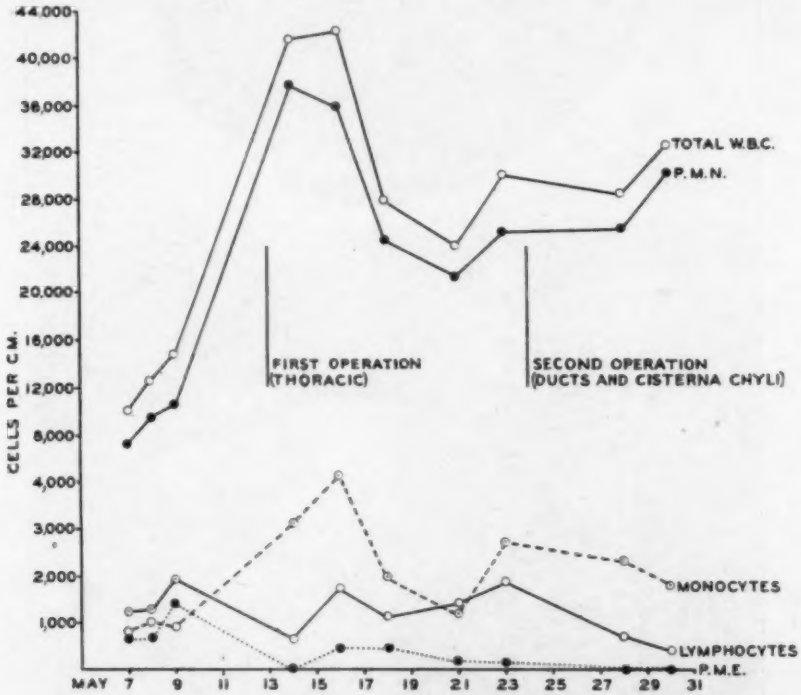

Fig. 3.—Curve showing data on the blood of dog 28. Note particularly the extremely low level of lymphocytes and eosinophils at the end of the experiment.

dilated; it contained coagulated material which could not be expressed. A needle was inserted into the thoracic duct, but fluid could not be forced into the system. The mediastinal lymph nodes were enlarged and edematous.

During the course of the experiment the weight of the animal showed a progressive loss from 11.75 to 6.79 Kg. After the operation on the lymphatic ducts there was a marked change in all the blood elements (fig. 5 and table 5). This change remained fairly constant, though slightly progressive, until the death of the animal. Both the lymphocytes and the eosinophils decreased to an extremely low level; this decrease was slowly progressive until the cells had practically disappeared from the blood stream. The monocytes, while extremely irregular in number, increased to an average of approximately three times the preoperative level, and

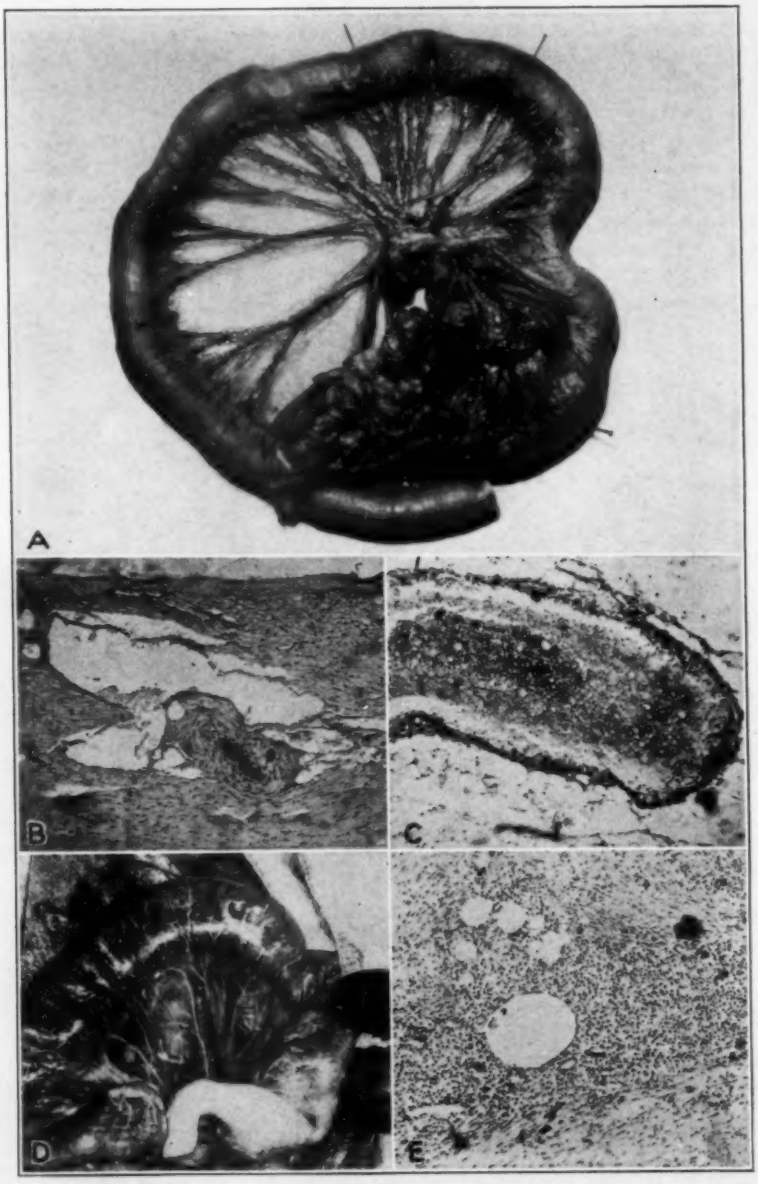

Fig. 4.—*A*, photograph of the small intestine of dog 15, showing mesenteric lymph vessels as large white cords filled with solid material. *B*, photomicrograph of a section of the heart of dog 15, showing distended perivascular lymphatics beneath the epicardium; × 50. *C*, photomicrograph of a section of the mesentery of the small intestine of dog 15, showing the lymphatics distended with coagulated lymph; × 50. *D*, photograph of the small intestine of dog 121, showing the extravasation of chyle into the intestinal wall. *E*, photomicrograph of a section of the lymph nodes of dog 121, showing small residual lymphatics in a mass of reticular tissue; × 50.

at the termination of the experiment were at the highest peak. There was also a marked increase in neutrophils. The correlation between the decrease in lymphocytes and the fall in eosinophils was extremely dramatic in this experiment.

The section in figure 4*C* was taken from the mesentery of the part of the intestine shown in figure 4*A*. In this area all of the lymphatics were filled with a coagulum containing cellular débris and a few lymphocytes. In figure 2*D* is shown a section from a lymph node which was markedly edematous and in which the lymphoid tissue was widely separated, markedly diminished and compressed. In figure 4*B* is shown tremendously dilated perivascular lymphatics in the cardiac muscle just under the epicardium.

Dog 121.—The operative procedures on dog 121 included a direct attack on the intraperitoneal lymphatics. It should be stated that it is much more difficult

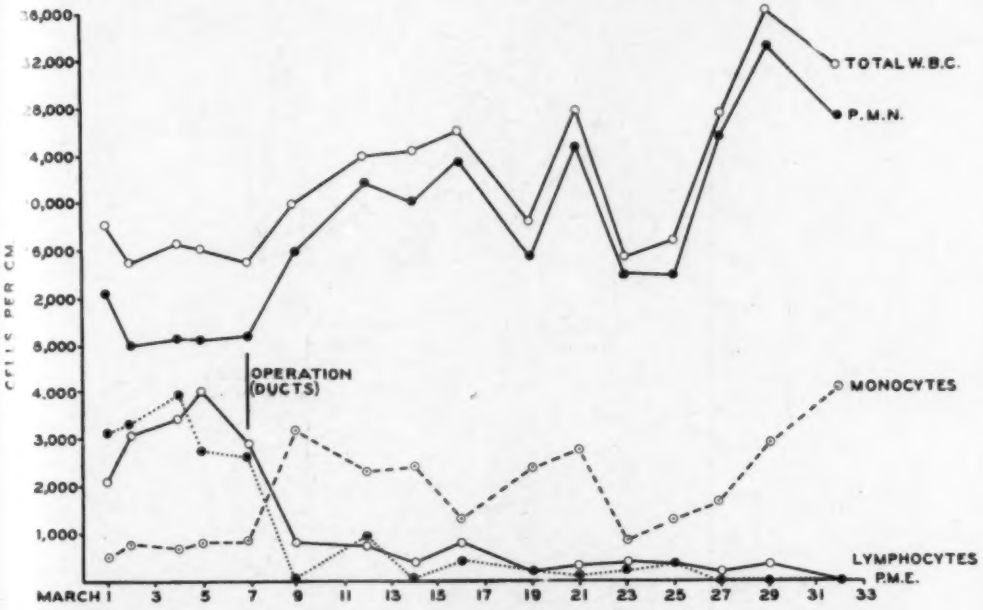

Fig. 5.—Curve showing data on the blood of dog 15. Note particularly the sharp fall in lymphocytes and eosinophils after ligation of the ducts and their progressive diminution to the end of the experiment.

to evaluate the results when such a method is used. This is due in the main to the fact that the manipulation, plus the sclerosing solution, results in numerous adhesions between the various coils of intestines. In the presence of marked blockage of the lymph vessels, the diffuse scarring prevents a striking picture such as that seen in dog 28, in which the lymphatics of the peritoneal cavity had not been attacked directly. The first operation on dog 121 was performed on Sept. 26, 1935. The weight of the dog was 7.4 Kg. Six days later the peritoneal cavity was entered, and 15 cc. of sodium morrhuate was injected into the mesenteric lymphatics and into the lymph vessels in the neighborhood of the inferior vena cava. Three days later, October 5, an incision was made in the left flank, and the cisterna was visualized. The cisterna was filled with coagulated material. It was freed from the surrounding tissues and removed. Free chyle could be seen through

the peritoneum in the abdominal cavity. An opening was made in the peritoneum, and some of the chyle was removed for study. Many dilated lymph vessels which were filled with chyle were seen. Extravasated chyle was noted to be present in the wall of the intestines. The incision in the flank was closed. Three days later, October 8, the animal was given 100 cc. of cream by stomach tube; samples of blood for determination of the fat content were withdrawn at intervals of thirty minutes for six hours. The results will be reported in a later communication.

The weight of the dog on October 10 was 6.77 Kg. The animal appeared to be in good condition. An abdominal incision was made with the animal under ether anesthesia, and the peritoneal cavity was opened. There was an enormous dilatation of the lymph vessels of the intestine which were filled with chyle (fig. 4*D*). Some

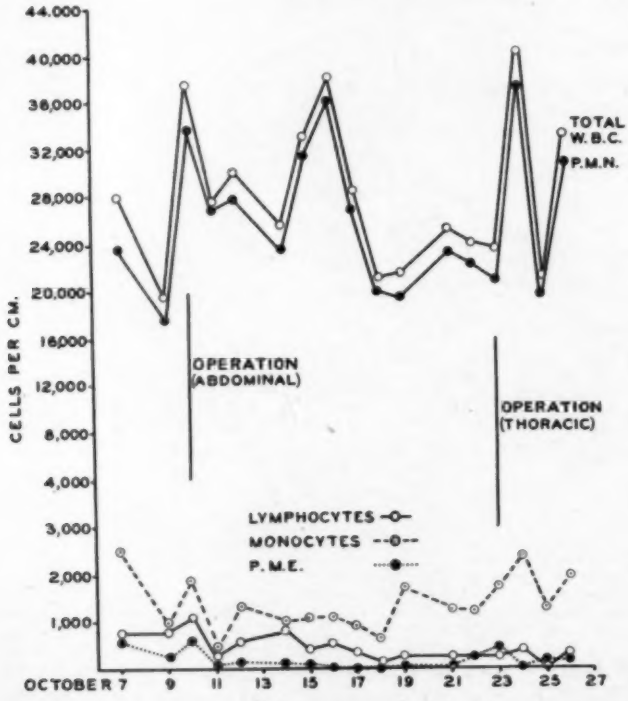

Fig. 6.—Curve showing data on the blood of dog 121. There were no preliminary counts, as three operations had preceded the first shown on the chart. Nevertheless, there was a definite change in lymphocytes and eosinophils following the obstruction of the abdominal lymphatics.

portions of the wall of the intestine were white, due to extravasated chyle. This is shown in figure 4*D*. Other parts of the intestinal tract could not be visualized owing to the numerous adhesions. Some chyle was extravasated in the omentum, but the alterations were not as marked as those in dog 28. There was a large lymph vessel filled with chyle lying on the anterior surface of the left kidney. Four cubic centimeters of sodium morrhuate was injected into the mesenteric lymph vessels, and 3 cc. was introduced into pelvic lymph nodes. The abdominal incision was closed.

Seven days later, October 17, the weight of the dog was 5.73 Kg. The temperature was 103.4 F., and the pulse rate was 150. The appetite was good. Three days later, the body weight was 5.5 Kg. An incision was made in the lower part of the left side of the chest, and the operation of Lee, plus the division of the mediastinal pleura, was carried out. On October 26 the dog appeared to be ill. The temperature was 103.5 F., the pulse rate 150 and the weight 5.44 Kg. Aspiration of the chest yielded 70 cc. of blood-tinged fluid. The dog had a soft stool, which was very light in color.

No preliminary blood counts were made on dog 121, but the counts made on October 7, which was two days after the third operation, showed an extremely low level both in lymphocytes and in eosinophils (fig. 6). During the next three weeks there was a slowly progressive decrease in the lymphocytes, the eosinophils remain-

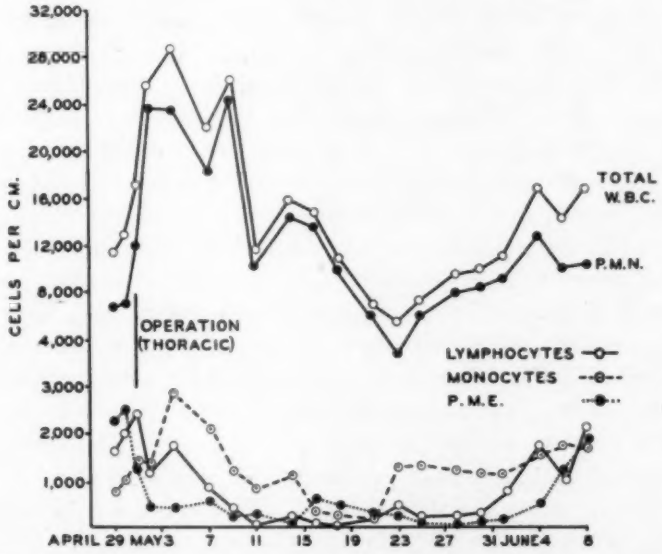

Fig. 7.—Curve showing data on the blood of dog 49. The fall in lymphocytes and eosinophils after the thoracic operation indicates obstruction, while the return to normal indicates the development of collateral circulation.

ing at a low level and being occasionally absent from the blood stream. There was a slow but progressive increase in the monocytes which, however, never reached an extremely high level. The fourth and fifth operations (as shown in figure 6 and table 5) apparently produced slight exacerbations in the slowly progressing change in the eosinophils and lymphocytes.

On October 26 it was believed that the animal would live less than twenty-four hours, and it was therefore killed. Most of the mesenteric lymphatics seen were hard white cords, but others could not be visualized, owing to the diffuse scarring and adhesions. The blood was removed from the vessels by means of a cannula, salt solution being used to wash out the vessels. After this, berlin blue was injected into the mesenteric lymphatics. There was retrograde injection everywhere. No communications between the lymphatics and the veins were demonstrated by the injection of berlin blue, although a careful search was made for such openings.

In several of the other dogs the results were similar to those of the experiment last described (dog 121), but in none of them was the picture as striking as that in dog 28. There was evidence of some regional blockage of the mesenteric lymphatics in most of the experiments in which the procedures were carried out in the peritoneal cavity, but in most instances it was not complete. It was observed frequently that berlin blue would flow in the reverse of the usual direction when introduced into the mesenteric lymphatics.

The sodium morrhuate in some instances caused marked necrosis of lymph nodes. When the nodes were examined a considerable time after the injection of the sclerosing solution, they were extremely hard. The section in figure 4*E* is from a lymph node in which the effects of the sclerosing solution were relatively complete. A large amount of scar tissue was present, and the peripheral sinuses were almost entirely obliterated. It is extremely interesting to note that lymph channels remained open in many of these nodes. This observation may well account to some extent for the extreme difficulty encountered in obtaining complete blockage in lymph nodes by the introduction of sclerosing solutions. These alterations are in marked contrast to those observed in the experiments in which blockage was obtained without the direct attack on the intraperitoneal lymphatics and hence without the injection of sodium morrhuate into these vessels. In these studies the lymph nodes were markedly enlarged and edematous. No scarring was present. The lymph sinuses were scanty and widely separated by lakes of fluid (fig. 2*D*).

In figure 7 and table 5 the counts on the peripheral blood of dog 49 are presented. After the thoracic operation on May 1, 1935, there was a marked decrease in the lymphocytes and eosinophils, indicating temporary obstruction. A return to normal in the blood picture three weeks later indicated the establishment of collateral circulation. The results in this animal are typical of those obtained in the majority of the experiments. These results are entirely comparable to the findings of Lee.[5]

Owing to the fact that chylothorax develops in a higher percentage of cats than of dogs after occlusion of the superior vena cava, it was believed that these animals would be more suitable than dogs for the present study. That is, it seemed likely that there would be fewer collateral lymph vessels in cats than in dogs. Such, however, did not prove to be the case. Although the difference is not great, we have the impression that it is easier to produce lymphatic blockage in dogs than it is in cats.

In a previous report it was stated that chylothorax was not observed in the four experiments in which occlusion of the thoracic duct preceded ligation of the superior vena cava. Chyle was not found in the pleural

cavities in the experiments on six cats in this series in which attempts at blockage of the lymphatics was followed by occlusion of the superior vena cava. In one experiment the fluid was slightly whitish, but was not definitely chyle. This is in contrast to the experiments on cats previously reported in which chylothorax developed in fourteen of twenty-three animals in which ligation of the superior vena cava was the only operative procedure. In other words, it appears that chylothorax is much more likely to develop if ligation of the superior vena cava is not preceded by occlusion of the thoracic duct.

The question arises as to whether or not the sclerosing solution might be responsible for the alterations in the cellular composition of the blood. This point was tested by introducing sodium morrhuate into cats by the intravenous, intramuscular and intraperitoneal routes. The quantity injected was comparable to that used in the experiments on lymphatic blockage. Six such studies were performed. There was no alteration in the cellular picture in four of these. A slight decrease in the eosinophils and lymphocytes occurred in one of the experiments, and a somewhat more marked decrease in the eosinophils took place in the remaining study.

COMMENT

Any effort to evaluate these experiments must depend on the angle from which one approaches them. From the question of the lymphatic system being necessary to life, these experiments certainly indicate that when all of the evidence pointed to complete blockage, the animal was unable to survive. This does not, of course, explain the cause of death; it may have been due to a lowered resistance and a subsequent infection, as there is, of course, some evidence that the lymphatic system and the cells of the blood are concerned in the defense mechanisms of the body. The normal temperature and slow pulse of dog 15 certainly do not suggest infection. It is possible that in some animals, particularly animals like dog 28, death was due to injury of the tissue, which was secondary to blockage. Other explanations might be thought of to explain the direct cause of death; but it is obviously unsound to assume a necessity for such explanations, since at the moment we are dealing solely with a specific analysis of the necessity of the lymphatic system to life, and these experiments certainly speak in favor of such a thesis.

Analyzed from the point of view of the blood, these experiments indicate a close relationship between the lymphocytes and the eosinophils in terms of the effect of the operative procedures on their level in the circulating blood. It is obvious that the decrease in lymphocytes after obstruction of the lymphatics results directly by interference with the supply coming from the lymph nodes. The explanation for the sharp decrease in eosinophils is not at hand. It is true that the level of these

cells in the animals used in these experiments was abnormally high in terms of the usual concept. Whether a larger series of dogs and cats would demonstrate that we were dealing here with a group of animals having an unusually large proportion of eosinophils or whether these species always contain so many cells of this type is not certain. However, regardless of whether we were dealing with animals sensitized by foreign proteins or parasites or whether they were entirely normal, it is certain that obstruction of the lymphatics did markedly interfere with the maintenance of a normal level of eosinophils in the circulating blood.

It will be necessary to perform additional experiments before conclusions can be drawn in regard to the possibility of preventing the entrance of fat into the blood stream by lymphatic blockage. In the only experiment (dog 121) in which the studies of the fat in the blood have been completed, there was no evidence of the absorption of fat after the feeding of cream. In this connection, the loss in weight in two of the three animals in which satisfactory blockage was produced may be of interest.

After occlusion in cats of the thoracic duct in the chest, Lee [9] observed collateral lymph channels which connected with the intercostal veins, and in one experiment a communication with a lumbar vein was observed. Many lymphaticovenous connections in the abdominal region have been demonstrated in the present study, and by far the most common site is with the inferior vena cava in the neighborhood of the entrance of the renal veins. In this connection, the following experience is of interest. Several operations had been performed on a dog in an effort to produce lymphatic blockage. The studies indicated that collateral channels had opened up sufficiently to convey the lymph to the blood stream. In view of the fact that these connections were usually with the inferior vena cava after the operations in the neck, chest and flank, it was decided that the inferior vena cava should be ligated above the renal veins. This was done, and chylothorax ensued. More than 5 liters of chyle was aspirated from the chest during the seven weeks that the animal lived. Autopsy revealed a pericardium distended with chyle and large white solid masses of coagulated material.

It is interesting that preliminary ligation of the thoracic duct lessens the chances of the development of chylothorax after occlusion of the superior vena cava. The most likely explanation seems to be that the occlusion of the thoracic duct causes the opening up of collateral channels to veins other than the tributaries of the superior vena cava.

SUMMARY

Experiments have been performed on fifty-two dogs and twenty-two cats in an effort to produce complete blockage of the lymphatics. A total

of two hundred and sixty-seven operations were performed. A variety of operative procedures were carried out, but in general these have consisted of blocking the lymphatic ducts in the neck and chest, of destroying the cisterna and of interfering with the drainage of the mesenteric lymphatics. The cellular picture of the blood was determined frequently in most of the experiments both before and at varying intervals after the operation. In many of the animals there was undoubtedly temporary obstruction, which was relieved by the opening of collateral lymph vessels; in these animals there was a marked temporary change in the blood picture, with return to normal. The essential alteration in the blood consisted of a marked decrease in the eosinophils and lymphocytes. In most of the animals in which evidence of blockage disappeared, lymphatic communications with the inferior vena cava were demonstrated at autopsy.

The findings indicate that complete lymphatic blockage was produced in three dogs (28, 15 and 121). These experiments have been described in detail. There was an almost complete disappearance of the lymphocytes and eosinophils from the blood stream. The animals lost weight rapidly and were killed when it was obvious that they were going to die. The picture at autopsy was striking. The lymphatics of the abdominal organs were markedly distended, and there was an extravasation of chyle into many of the tissues. No lymphaticovenous communications were demonstrated.

ARTHROPLASTY IN THE LOWER EXTREMITY

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Arthroplasty is an operation designed to reestablish a useful range of motion in an ankylosed joint or to increase the mobility in a joint with restricted function. In one form or another it has been used for probably a hundred years, but the results until recently were only occasionally successful, and the operation was performed only by the most adventuresome. In this country the greatest stimulus for its modern application was provided by the careful work, encouraging results and enthusiasm of the late Dr. John B. Murphy. In the last two decades many of the problems of arthroplasty have been solved by the technical improvements evolved by orthopedic surgeons, notably, Allison, Baer, Putti, Campbell, Henderson and MacAusland. There is much work yet to be done in perfecting the operative procedures and in improving the results. But at present one can decide with fair accuracy the type of case in which the operation should be performed, and one may expect a satisfactory issue in the majority of such operations.

THE PROBLEM OF ARTHROPLASTY

At the outset the fact should be appreciated that primarily the aim of arthroplasty is to create in a pathologic area a normally functioning joint. It would likely enough be impossible for a surgeon to design and establish a perfectly functioning joint were he to deal with absolutely normal tissues. But when he endeavors to make a joint among and from abnormal tissue, with many essential structures, such as the joint capsule, the ligaments, the bones and the articular cartilage wanting, defective, scarred or contracted, there should be little wonder that the end-result is often disappointing. The problem of arthroplasty, therefore, must be approached with an appreciation of one's limitations, and one must not expect the newly constructed joint to be anatomically, physiologically and mechanically perfect. While the goal must ever be to approximate and to imitate the normal, one should feel gratified when arthroplasty yields a stable and generally useful joint.

Read before the New York Academy of Medicine, Section of Orthopedic Surgery, April 17, 1936.

THE CHOICE OF PATIENT

As arthroplasty is distinctly an operation of election and not of urgent necessity, great care must be exercised in the selection of the proper type of patient. Parenthetically, it should be noted that there is need also for some attention to the choice of a surgeon. Arthroplasty is admittedly a difficult operation, requiring on the part of the surgeon special dexterity, speed, an accurate knowledge of the pathologic anatomy of ankylosis, an understanding of the physiology and mechanics of the function of the joint, patience in attention to technical details both during and after the operation and last but not least, a devotion to the gentle handling of tissues. One can successfully perform arthrodesis of either the hip or the knee with considerable indifference to the articular and periarticular structures, but not so in arthroplasty. Consequently, no surgeon should undertake to perform arthroplasty unless he is by temperament and training fitted to do so. Now as to the choice of patient. First, the patient must enthusiastically desire the operation, for only under such circumstances will he submit to the requisite careful preparation and doggedly persist and cooperate in carrying out the details of the prolonged convalescence. Second, the patient should be within the age period of from 20 to 45 years. It is useless, at least on the basis of the present knowledge, to perform arthroplasty on a child, for aside from the technical difficulties and the danger of disturbing the epiphyses, with resultant retardation of growth, it will be impossible to obtain the patient's cooperation in voluntarily exercising the new joint, and ankylosis will inevitably recur. Similarly, the aged person is an unfavorable subject because he rarely possesses the stamina to resist the enervating effects of arthroplasty or the pertinacity requisite for exercising the member which has been operated on. I have in the last few years successfully performed arthroplasty of the hip for advanced hypertrophic osteo-arthritis or ununited fractures of the neck of the femur in persons 50 and 55 years of age. But, by and large, a patient under 45 is preferable to one over 45. Third, a very stout person is an undesirable subject by reason of the evident technical difficulties involved in the accurate execution of the operation. Fourth, the patient must be in good general condition and free from any active focus of infection, be it ever so distant or mild, in the sinuses, urethra, pelvis or bones. For in the presence of any such lesion there is great likelihood of an infection in the area operated on, and to hazard arthroplasty is to court failure. Fifth, the social and financial status must warrant the venture of arthroplasty. Remembering that the joint resulting from arthroplasty on the lower limb is far from normal, one must not expect that it can be subjected to severe strain. Hence arthroplasty is rarely indicated in a laborer, though I am not unmindful that there have been cases recorded in which the person operated on has been able to resume

laborious work. Certainly no one would expect that ditch diggers or structural iron workers would be able to return to their customary labor after arthroplasty of either the hip or the knee. They often do not do so after far simpler operative experiences. One can expect that the patient will be able to engage in light work. Consequently, those in the leisure and white collar classes and those with sedentary occupations are the most favorable subjects. Then, too, since the convalescence from arthroplasty usually extends over many months, with an average duration of probably no less than a year, the patient undergoing such an operation must have the funds and the opportunity for staying away from his work to devote himself, with peace of mind, to the serious business of the gradual reestablishment of the function of the joint.

THE PRINCIPLES OF ARTHROPLASTY IN THE LOWER LIMB

In planning arthroplasty on the hip or knee one aims to obtain not only motion but stability of the joint in order to permit secure weight bearing. Enough bone should be removed to allow easy gliding of the articular ends. The articular surfaces should be smooth and fit fairly accurately. The capsule of the joint should not be stripped up any more than is indispensable to a satisfactory exposure of the bones in order that it may give adequate and reliable support to the newly formed joint. Arthroplasty should not be performed on a limb that is greatly deformed. For instance, if a hip is ankylosed in marked adduction and flexion, it is advisable to correct the deformity, place the limb in a neutral attitude and require the patient to walk about for several weeks or even months, depending on the severity and duration of the deformity, before undertaking arthroplasty. Similarly, a knee that is markedly flexed ought to be straightened by stretching or osteotomy before arthroplastic mobilization. It is important, too, to have a good circulation about the joint. Therefore, if there is extensive scarring, as after a burn, or loss of bone or muscle tissue, as after a severe fracture or osteomyelitis, this should be corrected or improved by plastic repair. The condition of the muscles adjacent to the joint is a vital factor. In the presence of severe atrophy of the muscle there is little opportunity for voluntary exercise of the proposed joint. Preoperative massage and voluntary contraction of the para-articular muscles are excellent for building up the muscle tone and strength necessary for satisfactory postoperative function.

GENERAL INDICATIONS AND CONTRAINDICATIONS FOR ARTHROPLASTY OF THE HIP OR KNEE

Before arthroplasty is undertaken, the general indications and contraindications should be considered.

1. There should be a special need for motion in the ankylosed joint. A single ankylosed hip or knee not only may cause little inconvenience but may be adequately strong and resistant for ordinary activities. A banker, dentist or clerk with one ankylosed painless knee or hip can conduct his business affairs, be active socially and even engage moderately in gymnastic exercises. On the other hand, a professional dancer must have, and a person of leisure may earnestly desire, the maximum of mobility. In such persons arthroplasty is warranted even for ankylosis of one joint.

2. The ankylosed joint must be free from an active or even a latent process of infection. Spontaneous pain, local heat, tenderness to pressure over the joint and sensitiveness on manipulation of the limb preclude arthroplasty. Considerable discussion has arisen in regard to the advisability of reestablishing motion in an ancient apparently healed tuberculous joint. Cases have been reported, especially by Baer and Albee, in which the results were successful. In my service at the Hospital for Joint Diseases I obtained a most satisfactory result from arthroplasty on a knee that had become ankylosed following what appeared clinically to have been a tuberculous invasion. Yet the surgeon so often sees severe exacerbations in healed (?) tuberculous joints after minor injuries that he should hesitate to introduce the trauma that inevitably accompanies arthroplasty. Baer,[1] in a paper on arthroplasty of the hip, stated "that twenty-one of these cases were operated on before 1918, and only six since. In the series before 1918, one-third of the cases resulted in relighting the tuberculosis, although this has invariably quieted down, with a subsequent stiff hip." One should at the very least wait until the joint has remained healed for several years and has been subjected to prolonged weight bearing without any signs of recrudescence of the disease and without any evidence in the roentgenograms of cloudiness, rarefaction or bone absorption.

3. The most favorable cases for arthroplasty are those in which complete ankylosis has followed trauma, such as a fracture, or suppurative infection, either gonorrheal or pyogenic.

4. The most unfavorable cases are those in which rheumatoid arthritis is present. This is so because of the patient's poor healing qualities, the great tendency to recrudescence of the arthritis and the presence of so much atrophy at the articular ends of the bones that there is likely to be inadequate repair of the bone.

5. Eburnation of bone, extensive loss of bone or scarring and fibrosis of the muscles controlling the joint are decidedly contraindications to arthroplasty.

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1. Baer, William S.: Arthroplasty of the Hip, J. Bone & Joint Surg. **8**:769-802 (Oct.) 1926.

SPECIFIC INDICATIONS FOR ARTHROPLASTY OF THE HIP

When the hip is affected by any of the following conditions, arthroplasty is specifically indicated.

1. Ankylosis of one hip in a good attitude. By a good attitude is meant one in which the limb is slightly flexed, abducted and rotated outward. However, should the hip be in moderate flexion, say 30 degrees, and adduction of 15 degrees, the operation is not necessarily contraindicated. When there is marked deformity, as a right-angled contraction, it ought to be corrected by stretching or osteotomy and arthroplasty postponed for at least six months for two specific purposes: first, to make certain that the corrective manipulation has not lighted up a latent infection and, secondly, to allow the tissues, especially the bone, to accommodate their structures to function in the optimum position of the limb.

2. Ankylosis of both hips or involvement by a pathologic process which severely restricts motion. In this case one hip ought to be mobilized for improved function.

3. Ankylosis of both hips and both knees. If this deformity exists, one hip and the opposite knee should be subjected to arthroplastic procedures.

4. Hypertrophic osteo-arthritis of the hip occurring as an isolated idiopathic lesion and seen frequently in the third and fourth decades of life or as an end-result of a slipping of the epiphysis of the femur or of Legg-Perthes' disease. In such cases the active pathologic process has subsided, and there is no danger of reactivation. The head of the femur is greatly enlarged, but it can be pared down and shaped to resemble the normal bone. The cartilage in the floor of the acetabulum may be normal, or it may have been replaced by fibrous tissue which forms a favorable acetabular covering for the proposed arthroplasty. The margin of the acetabulum is sometimes encumbered with osteophytes, which can be excised fairly thoroughly. The capsule of the hip joint may be thickened but intact and can be preserved to assure stability. If the neck of the femur is shortened, it is advisable to combine with arthroplasty a Whitman reconstruction, the essential feature of which, for the purposes of this procedure, is a lowering of the great trochanter on the shaft of the femur to allow a satisfactory range of abduction. I have performed this type of operation, namely, a reconstruction arthroplasty, with great satisfaction.

5. Ununited fracture of the neck of the femur. In cases in which there is a sizable remnant of neck the effect of the Whitman reconstruction operation can be improved materially by surrounding the newly formed head and neck of the femur by a double layer of fascia lata. The result will improve both stability and the range of motion.

6. Ankylosing arthritis of the hip either as part of a generalized atrophic polyarthritis or as a complication of spondylitis deformans. Arthroplasty is specially indicated if both hips are affected.

SPECIFIC INDICATIONS FOR ARTHROPLASTY OF THE KNEE

Arthroplasty of the knee is specifically indicated when any of the following conditions are present:

1. Ankylosis of a single knee is complete extension or slight flexion resulting from an old pyogenic infection or a crushing fracture.

2. Ankylosis of both knees. In this condition at least one of the knees should be mobilized.

3. Ankylosis of both knees and both hips. When this condition exists, one knee and the opposite hip should be operated on to permit some function in the lower limbs besides standing.

4. Ankylosis of one knee as a result of a tuberculous infection. In this case arthroplasty should not be performed unless there is reasonable certainty that there is no residual disease of the bone, and the patient, after having had the hazards of the operation explained, chooses to assume the risk.

5. Rheumatoid arthritis. In this condition the ankylosis is incomplete, and the patient suffers from a painful limitation of motion. The prognosis of arthroplasty is only fair by reason of a usually coexisting polyarthritis, atrophy of the bones and the muscles, poor resistance with consequent liability to infection of the wound and the possibility of precipitation of an exacerbation of the old inflammatory process. Nevertheless, arthroplasty is warranted in selected cases in which motion in one knee is desired to permit increased physical activity and independence.

ARTHROPLASTY OF THE ANKLE

It is seldom that an arthroplasty of the ankle is contemplated or indicated. When only the tibio-astragalar joint is stiff there is enough elasticity contributed by the motions in the other joints of the foot to make walking fairly easy and comfortable. In those cases in which the tarsal joints as well as the ankle are ankylosed, as after a crushing injury or osteomyelitis, the tissues are so thoroughly distorted, the joint capsules and ligaments having been destroyed or ossified, that there is little opportunity for a successful operation.

TECHNIC OF ARTHROPLASTY

The principal feature of arthroplasty, after the proper molding and reshaping of the ends of the bones, is the interposition of a material to prevent contact and fusion of these ends. Many different substances

have been utilized, but it is, I believe, the consensus today that a double layer of autogenous fascia lata is the preferable medium to maintain separation of the extremities of the bones. In both the hip and the knee this double layer serves as a covering for the ends of the bones and provides a real joint space. The fascia should be carefully applied and securely fixed by a row of peripheral sutures which will assure its proper placement. That a new joint is actually formed is proved both by clinical experience and by the investigation of joints on which arthroplasty has been performed. Campbell opened up six such knee joints and found a true joint in every one. The interposed fascia became altered and acted as a synovial membrane. There was a definite joint space with synovial fluid. The articular bony surfaces were smooth and glistening and were covered with a fibrous tissue resembling the original fascia. The capsule was thickened. A section of fascia and bone examined microscopically revealed that beneath the fascia there was a layer of cartilage and fibrous tissue uniting it to the bone.

When fascia lata is not available, one can use a pedicled flap of muscle, fat and fascia, chromicized pig's bladder or prepared ox fascia. I have used both of the latter tissues but found that there was a greater hazard of postoperative infection and the liability of liquefaction and extrusion of the interposed tissue. It must, however, be remembered that the late Dr. William S. Baer used chromicized pig's bladder with remarkable success.

In no type of operation is it so imperative to observe the strictest asepsis as in arthroplasty, as infection spells failure. The technic must be as nearly atraumatic as possible. Every step of the operation must be planned in advance so that the tissues are not damaged unnecessarily. In particular, there should not be extensive stripping of the joint capsule, as that would weaken the joint and reduce the stability, which in the lower limb is of paramount importance. The control of hemorrhage is another important feature. In operating on the knee, an Esmarch bandage affords a bloodless field. In the hip all bleeders should be carefully clamped off or tied.

The method of approach to the joint is a matter of individual experience and preference. In the hip I like the half U or the anterior Smith-Petersen incision. Either gives a rapid and adequate exposure. In this joint I always form a ball and socket joint that approximates the normal joint. One must be sure to have a more or less capacious acetabulum, otherwise the friction of the bony surfaces will rapidly destroy the interposed fascia. If there is any remnant of the capsule of the hip, it should be retained and preserved. In the cases of osteoarthritis and ununited fractures, the capsule can be easily identified, incised and retracted without destroying its support after resuture at the termination of the operation.

In the knee several different incisions have been used. Baer used two vertical lateral incisions. Campbell approaches the joint through a curved anterior incision. Putti exposes the knee through an inverted Y incision. I prefer the median parapatellar incision, very properly called by Krida the general utility incision. In exposing the bones it is generally necessary to lengthen the quadriceps tendon. This can be done through a Z or inverted V cut into the tendinous portion of the rectus femoris muscle. The reformation of the knee can be attained through either of two current procedures. Putti, MacAusland and others, desiring to imitate the natural conformation of the knee, remodel the lower end of the femur into two condyles with an intercondyloid notch and the tibial extremity into two cup-shaped depressions with an intervening spinous projection to fit the condylar surfaces of the femur. Campbell and his followers perform an operation of convenience and practicality by modeling the lower end of the femur into a single condyle and shaping the tibia into an appropriate saucer-like depression. In my service at the Hospital for Joint Diseases the Campbell technic has been utilized with satisfactory results.

POSTOPERATIVE CARE

The postoperative care is almost important phase of arthroplasty. The primary requisite is immediate postoperative immobilization, which should be continued long enough to allow the tissues to recover from the operative trauma. This implies complete rest of the joint for a minimum of two weeks. The splinting is conveniently obtained by a plaster of paris spica bandage for the hip and a plaster of paris circular support or a brace for the knee.

In arthroplasty of the hip the limb should be fixed with the hip in flexion of 10 degrees and abduction of 25 degrees. It is well, also, to provide for traction under the plaster spica so that the newly formed articular surfaces may be kept separated. At the end of two or three weeks the spica is removed, and the limb is placed in a balanced swinging apparatus, either a Thomas brace or a plaster posterior shell. Passive and active exercises of the hip are initiated and carried out several times a day. Baking and massage of the hip and thigh reduce the postoperative edema and sensitiveness and favor function. The motion at the hip should be increased daily but should always be retained within a painless range. The limb should never be stretched or moved violently. After eight weeks the patient is fitted with a Thomas Caliper brace with a half-ring for support of the ischium. He now begins to walk with the aid of crutches and is encouraged to be about daily for increasing periods. The brace may be discarded in from four to six months, provided there is no pain on moving the hip or during weight bearing. The crutches may be replaced by a cane, which is used for a variable period. Physical therapy is advantageously continued for about a year.

In the case of the knee the original support, holding the knee in about 30 degrees of flexion, is left undisturbed for two weeks. The limb is then supported in a balanced jointed plaster splint or a Thomas brace with a Pearson attachment. Physical therapy is applied daily, and the patient is encouraged to move the knee. At the end of eight weeks the limb is fitted with a caliper brace and an ischial ring, and the patient is allowed out of bed for brief periods every day, being encouraged to walk with the aid of crutches. Gradually the crutches are replaced by a cane. At the end of about six months, if the knee is stable and painless, the brace may be left off and the amount of exercise slowly increased.

Arthroplasty is applied to joints that are either completely or partly ankylosed. In the latter group may be included hip and knee joints affected with rheumatoid arthritis and hips in which there is a hypertrophic osteo-arthritis. I have operated on eighteen hips disabled by hypertrophic osteo-arthritis. A detailed report of this experience will be published in a separate communication. The results have been encouraging. In fifteen of the eighteen cases there was either a good or a fair result, each patient having a stable hip, no pain or very little discomfort and a variable but satisfactory range of movement. In the remaining three cases, the result is unknown in two, and one patient died while at home about three weeks after the operation with symptoms suggestive of a pulmonary embolism. In some cases of hypertrophic osteo-arthritis the neck of the femur is very short. Consequently, in order to assure adequate abduction I have lowered the attachment of the trochanter on the shaft of the femur. I described this combination operation, that is, the reconstruction-arthroplasty, several years ago before this section. The satisfactory results of arthroplasty in cases of hypertrophic osteo-arthritis of the hip become particularly interesting because of the large number of such patients who seek relief from the condition.

CONCLUSIONS

1. Arthroplasty in the lower limb is useful in selected cases of ankylosis of the hip and knee.

2. Great care must be exercised in selecting both the proper type of patient and the proper type of joint to be operated on.

3. Arthroplasty requires meticulous attention to the operative technic and the postoperative therapy.

4. The best result is obtained by arthroplasty on a patient who has a single joint ankylosed from a crushing trauma or a pyogenic infection.

5. In cases of ankylosed healed tuberculous joints arthroplasty may be successful, but there is always the danger of lighting up a latent infection.

6. As reconstruction-arthroplasty, the operation may be employed in cases of ununited fractures of the hip.

7. Arthroplasty may be used with fair success on joints that are partly ankylosed from rheumatoid arthritis.

8. In cases of hypertrophic osteo-arthritis of the hip an arthroplasty or reconstruction-arthroplasty yields unusually good results.

Fig. 1 (case 1).—Anteroposterior and lateral views of the right knee, taken on May 26, 1934, about one and one-half years after arthrodesis. Solid bony union and complete eradication of the joint are shown.

REPORT OF ILLUSTRATIVE CASES

CASE 1.—Benno L. was admitted to my service at the Hospital for Joint Diseases on Oct. 22, 1932, at the age of 19. He had a painful swollen right knee. The history showed that he had injured the knee when 2½ years of age. He recovered from this injury. But at the age of 10½ he hurt the knee again, with consequent pain, swelling and stiffness of the joint, necessitating the use of a brace for over a year. Eighteen months before admission to the hospital he hurt the knee a third time, and since then the knee had been painful, swollen

Fig. 2 (case 1).—Anteroposterior and lateral views taken fifteen months after arthroplasty. There is a wide joint space. The articular surfaces appear very irregular in the anteroposterior but not in the lateral view.

Fig. 3 (case 1).—Photographs made on March 11, 1936, twenty-one months after arthroplasty. These show a range of 90 degrees of flexion.

and flexed. During the past year he walked only with the aid of crutches. The roentgenograms showed marked erosion of the articular ends of the femur and tibia. The history of the repeated attacks of disability and the existence of erosion of the bone led to the diagnosis of tuberculosis of the knee.

On October 28 arthrodesis of the knee was performed. At operation softening and erosion of the bone were evident. There were no abscesses. The culture and microscopic examination of the removed tissue did not reveal any tubercles or tubercle bacilli. The result of the operation (fig. 1) was most

Fig. 4 (case 2).—Preoperative roentgenogram showing marked osteo-arthritis. The head of the femur is enlarged, flattened and irregular and probably represents an end-result of slipping on the epiphysis of the femur or of Legg-Perthes' disease.

satisfactory, as the patient obtained a solid fusion of the tibia and femur. Subsequently he became desirous of having his knee mobilized. This ambition was encouraged for the following reasons: First, an absolutely positive diagnosis of tuberculosis was not established. Second, since the knee had been fused he had been able to walk liberally and has had no discomfort in the knee and no sign of relighting of the inflammatory process. Third, the roentgenogram showed solid bony union and no areas of rarefaction, absorption or proliferation of bone.

In June 1934 he was readmitted to the hospital, and arthroplasty was performed through a median parapatellar incision. The Campbell technic was used; that is, a single condyle was prepared at the lower extremity of the femur and the tibia was modeled into a single saucer-like depression. The patient had an uneventful convalescence. Roentgenograms (fig. 2) made in September 1935 showed an extensive joint. The articular surfaces appeared somewhat irregular, but the function was satisfactory. Photographs (fig. 3) made in March 1936, nearly two years after arthroplasty, showed the presence of 90 degrees of motion

Fig. 5 (case 2).—Postoperative roentgenogram, showing reshaping of the head and neck of the femur. The articular surface of the head is fairly even and smooth. The irregular mass of bone above the neck of the femur is extra-articular.

in the knee. The patient walks without pain and without a limp and is able to stand on the operated leg—despite the fact that there is some lateral motion in the knee.

An interesting feature in this case is that, although the patella was not available at arthroplasty since it had been used at arthrodesis as a graft to favor fusion of the tibia and femur, this did not interfere with the ultimate function of the knee.

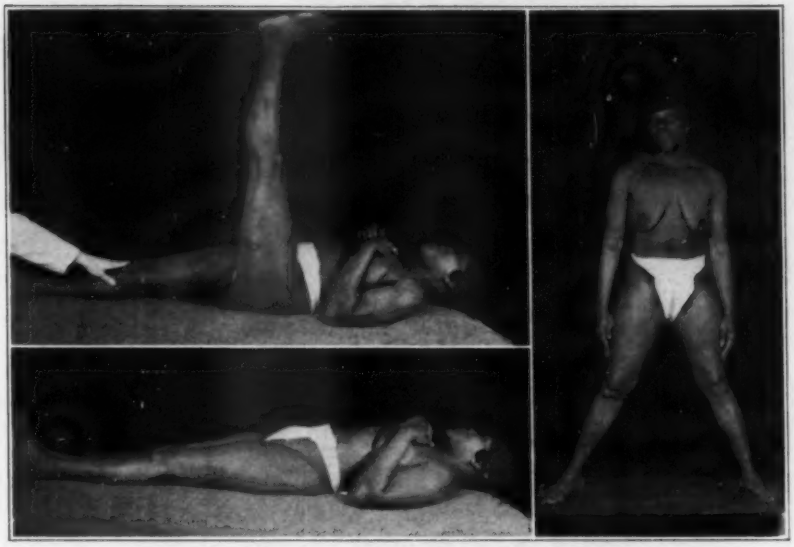

Fig. 6 (case 2).—Photographs made twenty-one months after arthroplasty. These show normal extension, flexion to 90 degrees and abduction to 30 degrees.

Fig. 7 (case 3).—Preoperative roentgenogram of the left hip, showing marked osteo-arthritis.

Fig. 8 (case 3).—Postoperative roentgenogram taken seven months after arthroplasty. The newly formed head of the femur, while small, is smooth and lies in a roomy acetabulum.

Fig. 9 (case 3).—Photographs showing the range of motion in the left hip after arthroplasty performed three years and three months previously.

CASE 2.—Gladys H., aged 33, was admitted to my service on June 4, 1934. Her chief complaint was pain in the left hip. This had started about six years previously and had continuously increased so that she was quite disabled at the time of her admission. Examination showed that the left lower limb was fixed in an attitude of 150 degrees of flexion and 10 degrees of adduction at the hip. There was no abduction and only a slight range of rotation. The roentgenogram (fig. 4) showed osteo-arthritis of the hip. The head of the femur was irregular and greatly enlarged, and the neck was shortened. The appearance suggested a late result of either slipping of the epiphysis of the femur or Legg-Perthes' disease during childhood.

Arthroplasty was performed on June 8 through an anterior Smith-Petersen incision. The patient had an uneventful convalescence and was discharged from the hospital on August 15, nine weeks after operation, walking with a caliper brace and crutches.

A roentgenogram (fig. 5) made on March 30, 1936, showed a good hip joint. The head of the femur, much reduced in size, lay completely within the acetabulum. There was an irregular mass of bone above the neck of the femur. This, according to other views, was extra-articular and seemingly did not interfere with motion.

The patient was reexamined on March 30. She stated that she had practically no pain in the hip and that she was pleased with the result of the operation because she can walk as much as she wishes, climb stairs, does all her own housework, including scrubbing of floors, and has, since the operation, been pregnant and delivered of a normal baby without difficulty. She walks without a limp. The original deformity is gone. She now has complete extension of the hip, flexion to 90 degrees, abduction to 30 degrees and a nearly normal range of rotation (fig. 6). There is ½ inch (1.3 cm.) of shortening of the left lower limb.

CASE 3.—William M., aged 38, was admitted to my service on Jan. 15, 1933, complaining of a painful disability in the left lower limb. Examination showed that he walked with a marked limp. The left lower limb was flexed and adducted at the hip. He had a range of flexion from 155 to 110 degrees. He had no abduction and no rotation. A roentgenogram (fig. 7) of the left hip showed marked osteo-arthritis. The joint space was almost completely obliterated, the head of the femur was enlarged and there was some hypertrophy of the bone at the rim of the acetabulum.

Arthroplasty was perfomed on Jan. 20, 1933. Chromicized pig's bladder was used to envelop the newly formed head of the femur. The patient had an uneventful convalescence and was discharged from the hospital on March 21, two months after the operation. On October 17, seven months after the operation, a roentgenogram (fig. 8) showed a small but smooth head of the femur in a capacious acetabulum. The neck of the femur was very short. The function at the hip was satisfactory.

The patient was reexamined on March 30, 1936, three years and three months after arthroplasty. For the past two and one-half years he has been working as a deck hand on a ferry, doing laborious work. He works from eight to ten hours a day without feeling exhausted. He walks up and down stairs without any difficulty. He has a slight limp. He sits down and gets up from a chair with ease. He can extend the hip to 170 degrees, flex it to 125 degrees, abduct and adduct about 15 degrees and rotate the limb a few degrees inward and outward. The mobility of the hip is shown in figure 9.

PAINFUL COCCYX

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In 1859 Simpson dignified persistent pain in the coccyx with a new and since popular term, "coccygodynia." Unfortunately, coccygodynia is descriptive in an anatomic and a symptomatic sense only and discourages diagnosis on an etiologic basis. "The Standard Classified Nomenclature of Disease" [1] classifies painful coccyx as due to infection (tuberculosis or osteomyelitis) or to trauma (fracture, dislocation and contusion and tear of ligaments). This diagnostic classification also places the responsibility of finding an explanation for the pain on the physician and, fortunately, does not permit him to use the old nondiagnostic symptomatic designation.

HISTORY

The first recorded coccygectomy was done by Jean Louis Petit [2] in 1726, for what was probably tuberculosis. Blundell [3] in 1840 advised resection of the coccyx for relief of pain of indeterminate origin. Nott [4] (1844) receives the credit for the first resection in this country, in a patient with "neuralgia" due to caries of the coccyx. Simpson [5] in 1859, as previously mentioned, described persistent pain in the coccyx as a separate entity under the term "coccygodynia." Von Scanzoni [6] in 1867, inspired by Simpson's article, devoted two pages in his textbook to coccygodynia. These articles laid the foundation for what amounted to

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Thesis submitted in partial fulfilment of the requirement for the degree of D.Sc. (Med.) from Columbia University, May 1936.

1. Logie, H. B.: Standard Classified Nomenclature of Disease, Compiled by the National Conference on Nomenclature of Disease, New York, Commonwealth Fund, 1935.

2. Petit, J. L.: A Treatise of the Diseases of the Bones, translated from the French, London, T. Woodward, 1726.

3. Blundell, J.: Principles and Practice of Obstetric Medicine, revised by A. Cooper Lee and Nathaniel Rogers, London, J. Butler, 1840.

4. Nott, J. C.: Facts Illustrative of the Practical Importance of a Knowledge of the Anatomy and Physiology of the Nervous System, New Orleans M. J. **1**:57, 1844.

5. Simpson, J. Y.: Coccygodynia and Diseases and Deformities of the Coccyx, M. Times & Gaz. **1**:861, 1859.

6. von Scanzoni, F. W.: Lehrbuch der Krankheiten der weiblichen Sexualorgane, Vienna, W. Braumüller, 1867.

a fad for coccygectomy, and for many years afterward it was a common operation. Nonoperative treatment, utilizing hot sitz baths, a soft cushion to sit on and massage, was revived following the fad for coccygectomy and used almost universally until after the turn of the last century. The nonoperative form of therapy again was not yielding satisfactory relief to many patients, and some surgeons once more advocated resection of the coccyx, while others stated that "operative removal of the coccyx was notably unsuccessful." Yeomans [7] wrote "that many methods of treatment have yielded varying degrees of success is the best evidence of their unreliability." In 1914 he presented a new method of treatment, which consisted of the injection of 70 to 80 per cent alcohol into the sensory nerves of the coccyx to cause their degeneration, as had been suggested by Schloessner in 1907 and practiced by him with marked success for the relief of neuralgia of the trifacial nerve. For those patients who were not relieved of their coccygeal pain after the injection of alcohol, Yeomans advised operative resection. Gant [8] in 1923 discarded the injection of alcohol and reported 90 per cent cures in 100 patients after coccygectomy. Suermondt [9] in 1931 wrote that epidural injections of procaine hydrochloride had relieved some of his patients of their coccygeal pain. Yódice [10] in 1932 and Kleckner [11] in 1933 injected 10 cc. of a 5 per cent solution of quinine and urea hydrochloride subcutaneously about the coccyx at intervals of one or two weeks, with relief from pain.

While a few other methods of relieving coccygeal pain have been reported, most surgeons have preferred nonoperative forms of treatment.

ANATOMY

The coccyx derives its name from the Greek word κόκκυξ meaning cuckoo, based on the resemblance of the coccyx to a cuckoo's beak. Colloquially, it is called the tail or crupper bone. The four coccygeal vertebrae are united in the adult to form the coccyx. While four is the usual number of these rudimentary vertebrae, occasionally there are five and rarely three. As age advances the various pieces become united with each other, the three lower vertebrae uniting before middle life and the

7. Yeomans, F. C.: Coccygodynia: Further Experiences with Injections of Alcohol in Its Treatment, Surg., Gynec. & Obst. **29**:612, 1919.

8. Gant, S. G.: Diseases of the Rectum, Anus and Colon, Including the Ileocolic Angle, Appendix, Colon, Sigmoid Flexure, Rectum, Anus, Buttocks and Sacrococcygeal Region, Philadelphia, W. B. Saunders Company, 1923.

9. Suermondt, W. F.: Die Behandlung der Coccygodynia, Arch. f. klin. Chir. **167**:671, 1931.

10. Yódice, A.: Treatment of Coccygodynia, Arch. argent. de enferm. d. ap. digest. y de la nutrición **8**:733, 1932.

11. Kleckner, M. S.: Coccygodynia: The Present Day Interpretation and Treatment, Tr. Am. Proct. Soc. **34**:100, 1933.

upper somewhat later, as a general rule. In advanced life the coccyx may join with the sacrum, the union occurring earlier and more frequently in the male than in the female. In general, the coccyx is a triangular osseous formation, the whole bone being curved in a forward direction; it is concave in front and continues the curve of the sacrum. A detailed anatomic description of the coccyx, except for the relationship of the coccyx to the rest of the pelvis, is not considered necessary in this paper, as it is readily available to those who are not already familiar with this body. This relationship must be considered separately in the male and the female pelvis as there is a distinct difference.

The bones in the female pelvis are more delicate than those in the male pelvis. The sacrum is shorter and wider and is less curved; the greater sciatic notch has a greater diameter; the ischial tuberosities are wider apart and everted; the inferior aperture is larger, and the coccyx is more movable and hence slightly more variable in position.

The greater sciatic notch is wider in the female than in the male pelvis. In measurements made by Caldwell and Moloy,[12] on a group of 70 dried pelves (35 male and 35 female pelves), the average width of the greater sciatic notch taken at its greatest diameter was 40.8 mm. for the male pelves and 53.9 mm. for the female pelves.

The sacrum tends to follow the posterior limb of the ilium or of the superior angle of the greater sciatic notch, and the coccyx tends to follow the curve of the sacrum. Therefore, in the male pelvis, with the narrow greater sciatic notch, the inclination of the sacrum and coccyx is forward into the pelvic cavity or tucked in between the ischia. In the female pelvis the greater sciatic notch is wider; consequently the inclination of the sacrum and coccyx is generally backward (figs. 1 and 2).

ROENTGENOGRAPHIC STUDY

Roentgenograms of the pelves of 262 patients who had complained of pain in the coccygeal region were studied. Studies were also made of 100 males and 100 females who did not complain of a painful coccyx but who had had roentgenograms made because of symptoms referable to the lower part of the back. The lumbosacral area was studied to ascertain if there was any common variation usually associated with a painful coccyx. All of the roentgenograms were examined with particular reference to the coccyx (table 1).

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12. Caldwell, W. E., and Moloy, H. C.: Sexual Variations in the Pelvis, Science **76**:37, 1932; Anatomical Variations in the Female Pelvis and Their Effect in Labor, with a Suggested Classification, Am. J. Obst. & Gynec. **26**:479, 1933.

The percentage of variations in the lumbosacral joint was about the same in the two groups of patients; consequently no common variation is associated with a painful coccyx.

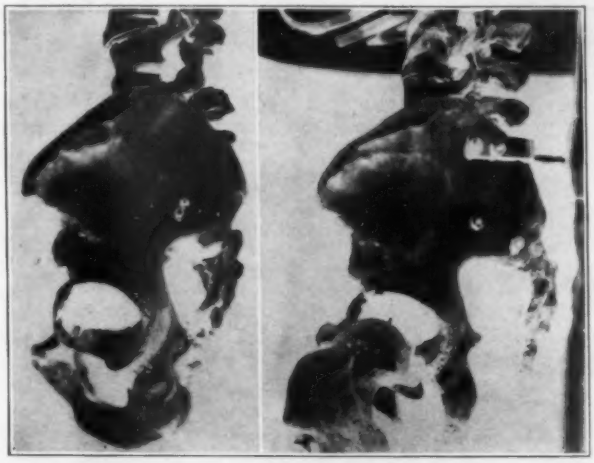

Fig. 1.—Photographs showing the variation in the width of the sciatic notch in the male and the female pelvis; also the position the coccyx assumes in relationship to the rest of the pelvis.

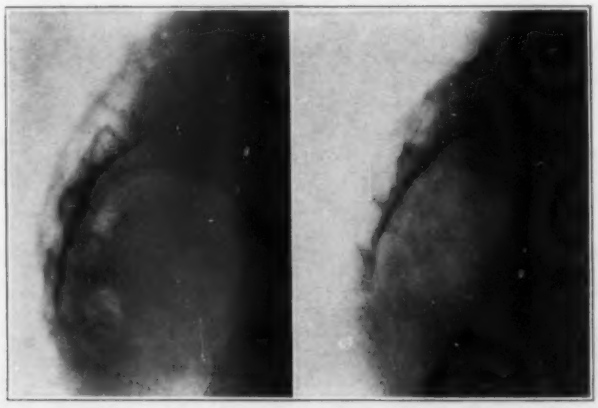

Fig. 2.—Lateral roentgenograms demonstrating the same anatomic relationship of the coccyx to the rest of the pelvis.

Malformations of the coccyx exist as the result of congenital influences and trauma, while variations are the result of congenital influences alone (table 2).

The number of coccygeal segments is variable, but four is the most common number. The number of segments found in the roentgen-

ographic study was approximately that found by Dieulaffe [13] in his osteologic study. He found 4 coccygeal vertebrae present in 79 per cent, 5 segments in 17 per cent and 3 segments in 4 per cent of 136 coccyges examined.

Roentgenographic findings are not significant in the explanation of painful coccyx except when a fracture, dislocation or osteo-arthritis is

TABLE 1.—*Variations in the Lumbosacral Joint*

Roentgenographic Picture	Absence of Painful Coccyx*	Painful Coccyx†
Unstable lumbosacral joint due to the following: Asymmetrical articulations, exaggerated lumbosacral angle, anteroposterior articulations	138 (69%)	156 (61%)
Unstable lumbosacral joint with posterior displacement, fifth lumbar on first sacral	36 (18%)	60 (22%)
Transitional lumbosacral joint (incomplete stabilization)	16 (8%)	26 (9.5%)
Spondylolisthesis	10 (5%)	8 (3%)
Lumbosacral area not shown on film	0	12 (4.5%)

* There were 200 patients (100 males and 100 females) in this group.
† There were 262 patients in this group.

TABLE 2.—*Anatomic Features of the Coccyx on Roentgenographic Study*

Roentgenographic Picture	Absence of Painful Coccyx*		Painful Coccyx†
	Males	Females	
No. of coccygeal vertebrae:			
3 segments present	11	12	39 (15%)
4 segments present	85	86	217 (83%)
5 segments present	4	2	6 (2%)
Fusion of intercoccygeal and sacrococcygeal joints	6	4	8 (3%)
Fusion of sacrococcygeal joint	15	10	37 (14%)
Fusion of intercoccygeal joints	5	3	12 (4%)
Fusion of the intercoccygeal joints except between the first and the second vertebrae	22	19	45 (17%)
Transitional sacrococcygeal joint:			
Unilaterally	7	8	29 (11%)
Bilaterally	1	1	18 (7%)
Lateral deviation of the coccyx	13	13	42 (16%)
To right	5	6	25 (10%)
To left	8	7	17 (6%)
Acute angulation anteriorly (over 45 degrees) of coccyx on sacrum	4	6	17 (6%)
Fracture of coccyx	0	0	12 (4%)
Dislocation of coccyx	0	0	6 (2%)

* There were 200 patients (100 males and 100 females) in this group.
† There were 262 patients in this group.

present. Almost any variation of the coccyx except a fracture or a dislocation that is noted in a patient with a painful coccyx can be matched in a roentgenogram of the coccyx of a patient who has never complained of pain in the coccygeal region.

13. Dieulaffe, R.: Le coccyx; étude ostéologique, Arch. d'anat., d'histol. et d'embryol. **16**:41, 1933.

Figures 3, 4, 5, 6 and 7 show various anatomic features of the coccyx as seen in roentgenograms.

To obtain good roentgenograms of the coccyx it is advisable to insist on the lower bowel being evacuated before making the plate, in order that fecal and gas shadows may not obscure the coccygeal field.

ETIOLOGY

Painful coccyx generally occurs after the age of 30 but may occur any time after puberty. In this series 7 per cent of the patients were under 20, 84 per cent between 20 and 50 and 9 per cent over 50 years of age. The youngest patient was 14 years of age, and the oldest, 68. Ninety-seven per cent of the patients were females. Trauma is a prominent feature, 89 per cent of the patients giving a history of a

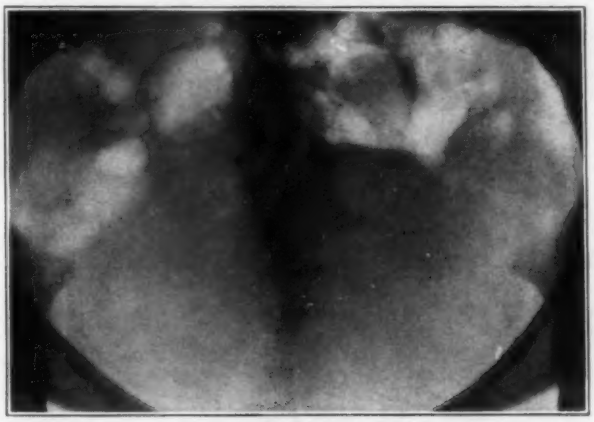

Fig. 3.—Anteroposterior roentgenogram showing the first coccygeal vertebra fused to the sacrum and the distal three coccygeal vertebrae fused as one piece.

fall preceding the onset of pain. In the remainder the onset of pain was insidious and may have been due to repeated small traumas of which the patient was unaware. Often coccygeal pain is but one part of the picture in a patient having generalized arthritis. A few instances of tuberculosis and osteomyelitis of the coccyx have been reported in the literature, but none has been seen in this clinic. Darrah,[14] Caubert [15] and David [16] have published reports of cases of tuberculosis of the coccyx, while cases of osteomyelitis of the coccyx have been men-

14. Darrah, R. E., cited by David.[16]

15. Caubert, H., cited by David.[16]

16. David, V. C.: Tuberculosis of the Os Coccygis, J. A. M. A. **82**:21 (Jan. 5) 1924.

tioned by Blount [17] and questionable cases, by Gaudier and Bertein [18] and Grisel.[19]

During a period when over 5,000 persons with tuberculous or osteomyelitic infections of the bones and joints were seen at the New York Orthopaedic Dispensary and Hospital not one had involvement of the coccyx. This is evidence of its extreme rarity.

Except in patients with fracture, dislocation, osteo-arthritis, sacralization, osteomyelitis or tuberculosis of the coccyx, there has been an absence of pathologic evidence to explain painful coccyx. Explanation of the pain that occurs in those patients who do not fall in the afore-

Fig. 4.—Lateral roentgenogram showing the marked anterior angulation of the coccyx on the sacrum.

mentioned classifications can be only theoretical. These theories are based on the following etiologic factors:

1. Infection, such as a local manifestation of a generalized infection.

2. Symptomatic pain, i. e., a referred pain of central origin due to functional or organic disease of the central nervous system, such as hysteria, neurasthenia, asthenia, the traumatic neuroses, tabes dorsalis and toxemia (Yeomans).

17. Blount, W. P.: Osteomyelitis of the Coccyx, J. A. M. A. **91**:727 (Sept. 8) 1928.

18. Gaudier, H., and Bertein, P., cited by Blount.[17]

19. Grisel, P., cited by Blount.[17]

3. Injury, contusions or sprains of the coccyx.

4. Postnatal injury, such as occurred in 12 cases from pressure of the fetal head on the terminal nerves of the sacral plexus (Graefe, reported by Yeomans).

Fig. 5.—Roentgenogram showing marked lateral deviation of the coccyx, due probably to a hemivertebra.

Fig. 6.—Transitional sacrococcygeal joint with sacralization on the left.

5. Neuralgic pain, i. e., that an initial trauma causes violent irritation of a nerve, which persists without any demonstrable lesion of the nerve (Marro, Pozzi and others, reported by Yeomans).

COMMENT ON ETIOLOGIC THEORIES

In regard to the first theory, the presence of arthritis is difficult to prove, but a painful coccyx in a patient with multiple arthritic joints is not uncommon and would lead one to suspect that the coccygeal pain is the result of the same factor or factors causing the generalized arthritis.

The second, or symptomatic, theory, in which the pain is considered due to any one of many functional or organic diseases of the central nervous system, has been the most widely accepted theory since painful

Fig. 7.—Anteroposterior roentgenogram showing a transitional sacrococcygeal vertebra with complete sacralization of the coccyx. The first coccygeal vertebra is fused to the sacrum, and the distal coccygeal vertebrae are fused as one piece.

coccyx has been thought of as a separate entity. Even in one of the most recent textbooks on neurology [20] there is a statement that "coccygeal neuralgia or coccygodynia is generally hysterical, and psychotherapy is the best form of treatment." The diagnosis of hysteria or neurasthenia is always dangerous and should never be made until all possible traumatic and organic lesions are ruled out. It frequently is

20. Wechsler, I. S.: A Textbook of Clinical Neurology, Philadelphia, W. B. Saunders Company, 1935.

an admission of defeat on the part of the physician. It is true that the complaint is most frequently found in females and that neurasthenia and hysteria are perhaps more often associated with this sex; however, the female coccyx is more prominent posteriorly and is easily exposed to trauma. One does not make a diagnosis of hysteria in cases of pain in the knee, ankle or any other joint after injury because one has come to recognize that ligaments and muscles may be partially or even completely ruptured. Why should one not judge the painful coccyx following injury on the same basis? Sprain of the sacrococcygeal or intercoccygeal joints does not differ from a sprain about the ankle or knee, except that the symptoms may be of longer duration. Sprained ankles or knees can be placed at rest, whereas the coccyx is almost always in motion and subject to repeated small traumas. The coccyx is an integral part of the floor of the pelvis and affords attachments to many perineal muscles; therefore, with every act of defecation or urination, and during the act of sitting or rising from a sitting position, movement takes place in the coccygeal joints. This continual motion tends to prolong the traumatizing factors for a longer period than is the case in the usual sprained joint.

It is also unlikely that a lesion of the lumbosacral or sacro-iliac joint would cause referred pain to the region of the coccyx. Pain referable to a lesion of the lumbosacral or sacro-iliac region occurs as frequently in the male as in the female. During 1934, 640 patients were admitted to the hospital complaining of pain low in the back, and of these, 321 were females and 319 males. Therefore, if a painful coccyx is always due to referred pain from lesions in either of these joints, the pain should be referred as frequently in the male as in the female. Painful coccyx is most often present (97 per cent) in the female. There is no direct nerve leading to the coccygeal area from the lumbosacral nerve plexus except that which supplies the gluteus maximus muscle, which, in turn, has a small area of origin on the coccyx. There might be some excuse for considering lesions of the sacro-iliac joint as causing referred pain to the coccyx, as the fourth and fifth sacral nerves are contiguous to that joint. While osteo-arthritis is common in my opinion, mechanical strains of the sacro-iliac joint are uncommon, and osteo-arthritis is seldom productive of pain because of the limited motion in this joint.

Of 200 patients who were admitted to the hospital during 1929 to 1934 for pain low in the back and who subsequently underwent an operation to produce spinal fusion, only 9 (8 of them females) complained of a painful coccyx. The status of the coccygeal pain in these 9 patients, at least two years after the spinal fusion, is as follows: One has no pain or tenderness referable to her coccyx; 1 still has coccygeal pain but has pseudarthrosis of the fused spine; 3 still have coccygeal

pain but also have general arthritic pains; 2 still have coccygeal pain (roentgenograms of their coccyx being normal and the spinal fusion solid), and 2 have been relieved by coccygectomy when their coccygeal pain persisted after spinal fusion.

Disregarding the patient who still has pseudarthrosis of the fused spine, there are 7 of the 8 remaining patients with a painful coccyx after the spinal fusion. This is further evidence that lesions of the lower part of the back are not a common cause of referred pain to the coccyx. Spinal fusion has not in our experience permanently cured or even alleviated painful coccyx, except possibly by the rest in bed in a recumbent position, which relieved the coccyx of direct pressure.

The remaining three theories are all based on traumatism, either trauma from within the pelvis or direct external violence, such as a fall in the sitting position. In the majority of the cases of painful coccyx the pain can be explained on the basis of one of these theories.

Pressure of the fetal head on the coccyx and its overlying soft parts has been reported to have caused a localized neuritis. This is certainly not a frequent occurrence, as one finds no reference to it in textbooks on obstetrics. Furthermore, the patients who have presented themselves to this hospital with coccygeal pain immediately after delivery constituted less than 3 per cent of the total group of patients having a painful coccyx.

Contusions of the coccyx and its surrounding soft parts and sprains of the sacrococcygeal joint are probably frequent. These contusions and sprains are usually caused by direct trauma, such as a fall in the sitting position. A fall in this position is more likely to traumatize the coccyx in the female because of lack of protection afforded by the ischial tuberosities, which are wider apart than in the male, and the deep posterior position the coccyx occupies in the pelvis, whereas in the male, with the coccyx tucked in between the two ischii, the force of the fall would be felt first by the ischial tuberosities and then by the prominent sacrum.

The coccyx is surrounded by compact, fibrous and muscular structures; within this fibrous and muscular network on both sides lies the coccygeal plexus of nerves, and on the anterior aspect of the coccyx are the two sympathetic ganglions. Therefore, any injury to the soft structures about the coccyx may damage the adjacent nerves, and they may be involved in the later stages of scar formation, thereby being the cause of persistent neuralgia of the coccyx.

While fractures and dislocations of the coccyx are not frequent, they do not differ in their symptomatology from any other fracture, subluxation or dislocation. The range of motion in the sacrococcygeal joint is so great, except in persons over 50 years of age, in whom this

joint is usually fused, that an extreme injury would be necessary to produce such a lesion. The direction of the force is usually upward or in line with the forward curve of the coccyx, and this affords added mechanical protection to the coccyx. A fracture or posterior dislocation of the coccyx caused by pressure of the fetal head has not, to my knowledge, been reported in the literature, although excision of a resistant coccyx to permit passage of the fetal head has been reported.[21] Several cadavers were placed in a prone position, and the coccyx was struck with a wooden mallet. This failed to produce a longitudinal fracture or dislocation and rarely caused a transverse fracture.[22] Gross

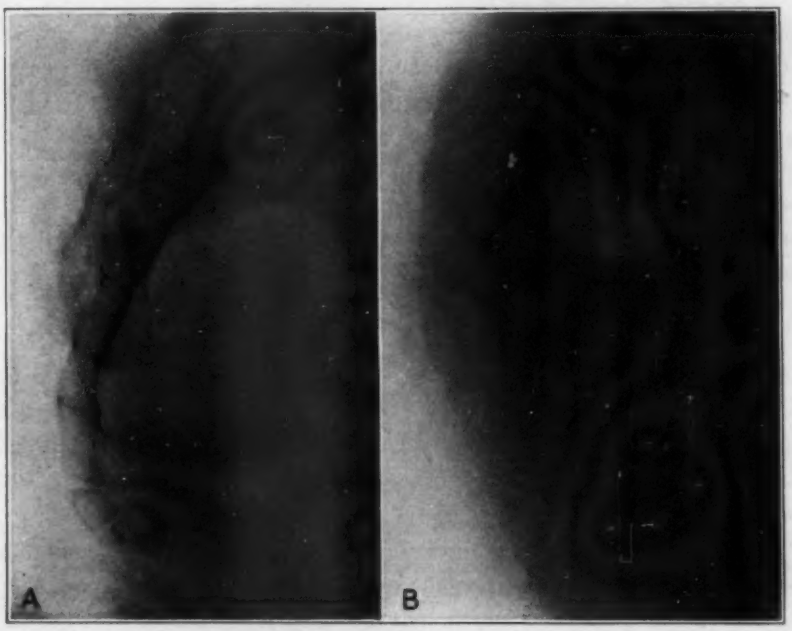

Fig. 8.—*A*, appearance of the coccyx before any local injury. *B*, dislocation of the coccyx anteriorly after a fall in the sitting position, in the same patient, one year later.

and microscopic examination of coccyges removed in this hospital for supposed fractures have failed to reveal any evidence of them (figs. 8 and 9).

21. Graff, E.: Resection of Coccyx During Labor, Wien. klin. Wchnschr. **37**: 1260, 1924. Heckscher, S.: Ossification of Coccyx as Obstacle to Delivery, Zentralbl. f. Gynäk. **52**:2886, 1928. Niedermeyer, A.: Resection of the Coccyx During Labor, Monatschr. f. Geburtsh. u. Gynäk. **86**:190, 1930.

22. Becker, F.: Zur unfallmedizinischen Bewertung der Frakturen und Luxationen des Steissbeins und der traumatischen Coccygodynie auf Grund klinischer und experimenteller Untersuchungen, Schweiz. Ztschr. f. Unfallmed. **25**:338, 1931.

SYMPTOMS AND SIGNS

Pain is localized to the coccyx or the surrounding structures. The pain is increased by pressure, such as that elicited on sitting or on palpation. On palpation the pain is most commonly caused by pressure from behind on the coccyx and the lower end of the sacrum rather than by pressure on the tip or from in front. Pressure exerted in this manner corresponds to the direction of the original injury. Contraction of muscles, as in the act of sitting or rising from a sitting position, is painful. Muscles attached to the coccyx in contracting flex it and in so doing stretch the tissues affected by the original trauma. Pain is at times present during defecation or urination. There is nothing significant in the character of the pain, as this is quite variable. Patients frequently sit with one side of the pelvis elevated to remove pressure from the coccyx. With the index finger in the rectum and the coccyx grasped between it and the thumb, tenderness can be localized, and the general contour, mobility, angulation and deviation, if present, of the coccyx can be determined. Any local pathologic process, such as thrombosed hemorrhoids, anal fissures, fistula-in-ano and prostatitis, can be determined at this time.

DIFFERENTIAL DIAGNOSIS

A pilonidal cyst is the most common lesion from which a painful coccyx is to be distinguished. With a pilonidal cyst there is usually a dimpling of the skin or a discharging sinus. No pain is elicited on rectal examination if a pilonidal cyst is present, as this lesion is entirely dorsal to the sacrum.

A tumor of the cauda equina sometimes causes referred pain to the coccyx, but there may be present as well sensory changes and saddle anesthesia and paralysis, which may be flaccid or spastic. The pain is worse when the patient is lying down but not when sitting. There is an increase in the protein content of the spinal fluid.

PROGNOSIS

The prognosis of painful coccyx is good. If nonoperative treatment is used recovery usually takes place in from two to four weeks after treatment is instituted. In some patients the recovery is slower, the pain gradually subsiding over a period of from four to six months.

During the past ten years only 30 (11 per cent) of 278 patients with a painful coccyx were operated on in this hospital. They were patients in whom nonoperative measures had failed to give relief. Resection of the coccyx yielded satisfactory results.

TREATMENT AND END-RESULT

From 1924 to 1934 278 patients were admitted to the outpatient department of the New York Orthopaedic Dispensary and Hospital with the complaint of pain in the coccyx. The average age of these patients was 34 years. Two hundred and sixty-seven (97 per cent) were females. Two hundred and forty-seven (89 per cent) recalled having received an injury to the coccyx, usually by a fall in the sitting position. Curiously, the most common cause of the fall in this group of patients was slipping on an icy pavement. The interval between the time of injury and the time of the patient's admission to the hospital for treatment varied from three days to six months. Usually from two to four weeks had elapsed.

Fig. 9.—Roentgenogram showing a longitudinal fracture through the transverse process of the first coccygeal vertebra.

All of these patients were treated nonoperatively either before admission to this hospital or afterward. Nonoperative treatment consisted first of all in improving the patient's posture, having her sit erect, and pull the buttocks in under the trunk, thereby taking the superincumbent body weight off the coccyx and causing the soft parts surrounding the coccyx to act as a natural cushion. This particular procedure is much more satisfactory than having the patient carry a small pillow or rubber ring or strapping the buttocks tightly together. All of the last mentioned procedures have been employed. Hot sitz baths for from twenty to thirty minutes twice each day proved of value. Constipation, when present, was relieved by suitable laxatives. Local massage has proved beneficial to many of these patients. Steady but firm stretching of the coccyx posteriorly has been done on patients for

several consecutive visits, with relief from pain. This is done to overcome the spasticity of the muscles having their insertion on the coccyx and to prevent the formation of adhesions and contractures in the sacrococcygeal joint and the surrounding coccygeal structures.

Local injection of 70 to 80 per cent alcohol has been found unsatisfactory. Epidural injections of both physiologic solution of sodium chloride and a 2 per cent solution of procaine hydrochloride have been used. The use of the former solution failed in every instance to relieve the local pain, while the use of procaine hydrochloride gave only transient relief, that is, for a few hours or until the effect of the anesthetic had worn off. Injections of 5 per cent solution of quinine and urea hydrochloride have been recommended but have never been tried in in this hospital.

Of the 248 patients treated by nonoperative methods, 54 were examined by me from one to four years after the onset of their coccygeal pain. In this group of patients only 2 continued to complain of a painful or tender coccyx. One of the common physical findings in this follow-up examination was that fusion of the sacrococcygeal and intercoccygeal joints had taken place in a large number of the patients, and in the remainder there was limited motion. This limitation of motion in the coccygeal joints, coeval with cessation of pain, is additional evidence that the coccygeal pain was coming from a lesion of the joint. Injection of alcohol about the coccyx may not cause degeneration of the coccygeal nerves, but by causing scar tissue to form it may so limit motion of the coccyx that the pain is diminished or cured. In both of the patients who continued to complain of coccygeal pain, motion at the sacrococcygeal joint caused an identical pain.

Relief from pain was experienced within one month after the injury by 36 (67 per cent) of the 54 patients, by 11 (21 per cent) within two months and by 5 (9 per cent) within six months, and 2 (3 per cent) continued to have a painful coccyx.

These results would seem to indicate that the nonoperative form of treatment should be tried for a period of six months before operative resection of the coccyx is resorted to. However, this preoperative period may be shortened if an increase, or no abatement, in the coccygeal pain occurs as a result of nonoperative measures.

Thirty (11 per cent) of the patients in the total group had operative resection of the coccyx. Of the 30 patients, 27 were females and 3 males, their average age being 32 years. The youngest patient was 15 years of age, and the oldest, 53. The average duration of symptoms before resection of the coccyx was eighteen months. Patients were followed on an average for two years after coccygectomy. The shortest follow-up period was two months, and the longest, five years.

RESULTS OF COCCYGECTOMY

Twenty-two patients (74 per cent) were completely relieved of coccygeal pain.

Three patients (9 per cent) had only partial relief from pain.

In G. K. calcification developed at the site of the coccygectomy, and there were also symptoms of generalized arthritis (fig. 10).

G. S. obtained only partial relief from coccygeal pain. No postoperative roentgenograms were available.

L. S. was followed for only two months. She moved to another city, and it has not been possible to locate her.

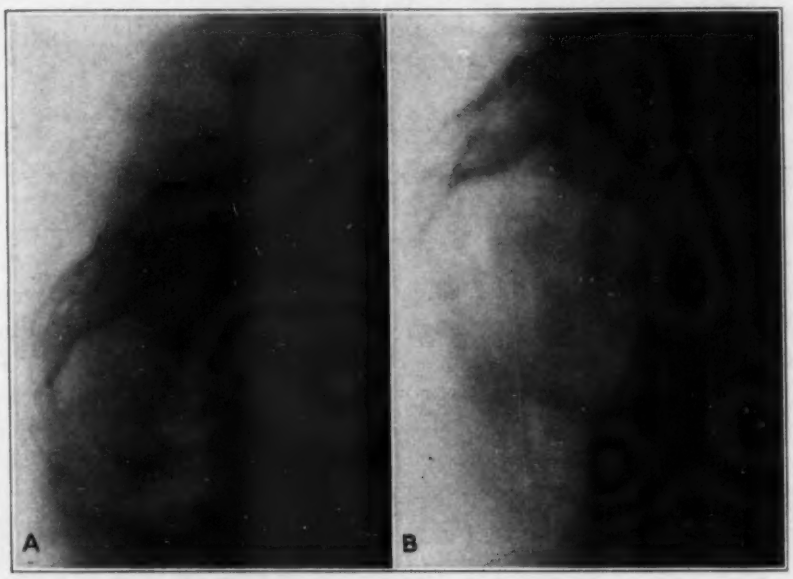

Fig. 10.—*A*, lateral roentgenogram showing the coccyx before operative resection. *B*, lateral roentgenogram showing postoperative calcifications at the site of the coccygectomy.

Five patients (17 per cent) were unimproved.

In M. H a local infection followed coccygectomy, and a sinus persisted for several months. Coccygeal pain continued, and nothing, including epidural injections of procaine hydrochloride (except temporarily), has relieved her pain. The pain is possibly caused by the coccygeal plexus of nerves being caught in scar tissue.

T. C. has continued to have coccygeal pain after coccygectomy. He also has a posterior displacement of the fifth lumbar on the first sacral vertebra, with an associated pain low in the back. Spinal fusion was advised, but the patient refused permission for the operation.

M. McK. underwent an operation for spinal fusion because of an acute lumbosacral angle and severely asymmetrical articulations. Coccygeal pain has persisted. The distal portion of the sacrum is prominent posteriorly, owing to the severe lumbosacral angulation.

M. B. has a calcified mass at the site of the coccygectomy, and coccygeal pain has persisted. The patient has refused to have this mass removed.

E. N. continued to have coccygeal pain for five months after operation, when she was last seen or heard from. There was no postoperative roentgenogram made of the site of the coccygectomy.

Nonoperative therapy, with the various methods adapted to the individual patient and applied vigorously and continuously, usually yielded satisfactory results. If coccygeal pain persists after from four to six months of this treatment, it is better to resect the coccyx.

COMMENT

Painful coccyx is so commonly the aftermath of an injury, such as a fall in the sitting position, that it is logical to consider the pain as due to local injury of the coccyx or its surrounding soft parts. Painful coccyx is most commonly seen in women, and an anatomic explanation has been presented to demonstrate that the coccyx is much more prominent posteriorly in the female pelvis and hence more liable to injury. The location of the pain is such that not only is it uncomfortable to the patient but she may neglect the condition for many weeks, as she may be loath to discuss such a lesion with her physician. There are a few other lesions that may localize the pain in the coccygeal area, but a careful physical examination can rule these out. The treatment should be nonoperative for a period up to six months. There is one exception to this, and that is a dislocation of the coccyx. When such a lesion is seen early the coccyx may be manipulated under anesthesia, and a reduction may be obtained. If nonoperative measures give but partial or no relief, the coccyx should be removed. Good results are obtained.

Painful coccyx is rarely of psychic origin, though neurasthenia may develop secondary to prolonged and severe pain.

300 Wainwright Building.

ARTIFICIAL MAINTENANCE OF CIRCULATION DURING EXPERIMENTAL OCCLUSION OF PULMONARY ARTERY

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Approximately one hundred and forty-two Trendelenburg operations for massive pulmonary embolism have been reported, and only nine of the patients operated on have left the hospital as cured.[1] This exceedingly high mortality is due to the critical condition of the patient and to the operative procedure, which entails the complete throttling of the great vessels leading from the heart for a brief period. Because of the difficulty in diagnosis and the uncertain prognosis, Nyström [2] advised postponing the operation until the patient is practically moribund. Then, as Churchill [3] has stated, "the procedure could perhaps be more properly termed an immediate postmortem examination than a surgical operation."

Nyström and Blalock [4] have demonstrated experimentally that occlusion of the pulmonary artery alone may be safely maintained for a longer period than occlusion of both the pulmonary artery and the aorta. Kiser [1] found that constriction of the afferent vessels of the heart in dogs allows a more prolonged interruption of the circulation to be safely carried out than occlusion of both the pulmonary artery and the aorta. This observation had previously been made by Läwen and Sievers [5] in 1910. On the basis of their experimental results, Jeger [6] in 1913 recommended compression of the venae cavae rather than the pulmonary artery and the aorta in the performance of the Trendelenburg operation. The

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From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

1. Kiser, W. J.: An Experimental Study of the Effects of Constriction of the Great Vessels of the Heart, Surg., Gynec. & Obst. **61**:765, 1935.

2. Nyström, G.: Experiences with the Trendelenburg Operation for Pulmonary Embolism, Ann. Surg. **92**:498, 1930.

3. Churchill, E. D.: The Mechanism of Death in Massive Pulmonary Embolism, with Comments on the Trendelenburg Operation, Surg., Gynec. & Obst. **59**: 513, 1934.

4. Nyström, G., and Blalock, A.: Contributions to Technic of Pulmonary Embolectomy: Experimental Study, J. Thoracic Surg. **5**:169, 1935.

5. Läwen, A., and Sievers, R.: Experimentelle Untersuchungen über die Wirkung von künstlicher Atmung, Herzmassage usw. auf die Lungenembolieoperation nach Trendelenburg, Ztschr. f. Chir. **105**:174, 1910.

6. Jeger, E.: Die Chirurgie der Blutgefässe und des Herzens, Berlin, August Hirschwald, 1913, p. 243.

clinical adoption of either of these principles, i. e., compression of the great veins or compression of the pulmonary artery alone, may diminish the hazard of the operative procedure, but the Trendelenburg operation will still remain a formidable undertaking.

A diminished cardiac output is the cause of death in massive pulmonary embolism.[7] Because of the obstruction in the pulmonary artery the heart cannot adequately continue its function of transferring blood from the venous to the arterial side of the circulatory system. Blood accumulates in the veins, and a greatly diminished amount of blood enters the left side of the heart. The aorta is inadequately filled by the output of the left ventricle, and the blood pressure falls. Figure 1 is a graphic illustration of this condition. The pulmonary artery of a cat was compressed by a clamp until the venous pressure rose and the arterial pressure fell. This simulates the condition of the circulation in a patient at the time of a Trendelenburg operation. If at this point some of the work of the heart in transferring blood from the venous to the arterial side of the circulatory system were assumed by a mechanical pump, one might expect an improvement in the condition of the circulation. The congestion of the veins would be relieved, and the greater flow of blood into the arterial system might be expected to produce a rise in the arterial blood pressure. If any considerable amount of blood were thus transferred from the venous to the arterial system through an artificial circuit, it would be necessary to rid the blood of its excess carbon dioxide and supply it with oxygen.

The requirements are in general those of an apparatus for perfusion of isolated organs or limbs with whole blood, but there are certain essential differences. Perfusion of an isolated organ is carried out through a cannula tied in the main artery of the organ. The blood returning from the organ is easily collected from the main vein. Finally, a relatively large supply of blood is required for the perfusion apparatus itself.

On the other hand, a temporary mechanical aid to the circulation of a whole animal involves the insertion of cannulas into relatively small peripheral vessels, the sacrifice of which will not preclude the resumption of normal cardiorespiratory functions by the animal's own heart and lungs. Furthermore, the volume of blood necessary to fill the apparatus should be relatively small, preferably only a small fraction of the animal's total blood volume. With these points in view, an apparatus was devised to test on experimental animals the feasibility of the hypothesis outlined. The procedure employed was as follows. Venous

7. Gibbon, J. H., Jr.; Hopkinson, M., and Churchill, E. D.: Changes in Circulation Produced by Gradual Occlusion of the Pulmonary Artery, J. Clin. Investigation **11**:543, 1932.

blood was obtained from a cannula in the right jugular vein. This venous blood was exposed to oxygen and then returned to the animal's circulation through a centrally directed cannula tied in the right femoral artery.

APPARATUS

The apparatus designed to oxygenate the blood has already been described.[8] The essential feature of the apparatus is a vertical revolving cylinder (fig. 2*A* and fig. 3). The stream of blood is directed at a tangent to the inner surface of the cylinder at its upper extremity. The revolution of the cylinder results in the distribution of a thin film of blood over its inner surface. The film moves downward by gravity, and the blood is collected in a stationary cup (*B*) at the bottom. The greater part of the space within the revolving cylinder is occupied by a hollow, closed, stationary cylinder (*C*), through the center of which passes a metal tube (*D*). A mixture of 95 per cent oxygen and 5 per cent carbon dioxide is conveyed through this tube to the bottom of the oxygenator. From here the gas

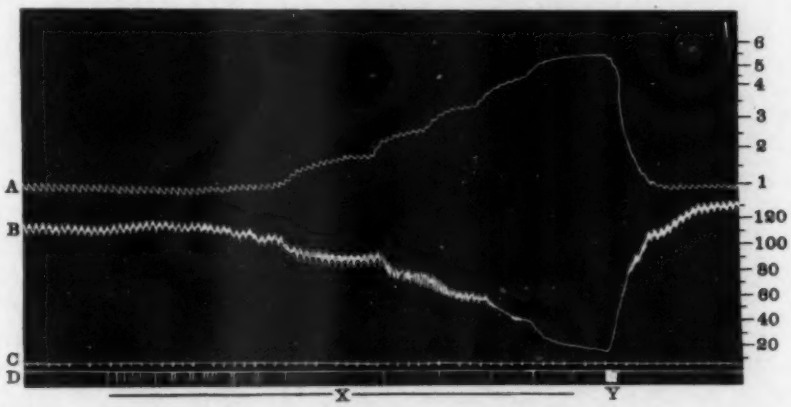

Fig. 1.—Kymographic tracing of the venous (*A*) and arterial (*B*) pressures during gradual complete occlusion (*X*) and release (*Y*) of the pulmonary artery. *C* is the time in five second intervals and *D*, the signal magnet. The figures to the right of the tracings represent the venous pressure in centimeters of water and the arterial pressure in millimeters of mercury.

passes up between the stationary and the revolving cylinders over the film of blood and escapes at the top. The apparatus was designed to meet the requirements of this particular problem. The ratio between the amount of oxygen introduced per minute into the blood and the volume of blood contained in the oxygenator is higher than in other oxygenators which have been described.[8] It accommodates a flow of blood of 500 cc. or more per minute, and large variations in the rate of flow do not produce foaming.

Blood was moved through the artificial circuit by two pumps (*E*, *E'*). One (*E*) transferred the blood from the venous cannula to the oxygenator, while the other (*E'*) returned the blood from the oxygenator to the arterial cannula. The

8. Gibbon, J. H., Jr.: An Oxygenator for Blood with a Large Surface Volume Ratio, to be published.

pumps were based on de Burgh Daly's [9] modification of the perfusion pump of Dale and Shuster.[10] The principal feature of each pump was a rubber finger-cot (*F*, *F'*), which was alternately compressed and expanded by air. The finger-cot was placed in the blood circuit between two valves (*G*), which directed the flow of blood. Expansion and compression of the air in the finger-cot chamber was accomplished by an air piston pump (*H*). A small air compressor pump (2 inch bore [5 cm.] and 1¾ inch [4.4 cm.] stroke) was converted to this purpose by removing the valve in the cylinder head and sealing the valve in the piston head. The outlet at the top of the cylinder was connected by rubber pressure tubing with a small air chamber surrounding the finger-cot. The downstroke of the piston decreased the air pressure in the closed system, and the finger-cot (*F*) expanded, drawing blood into it through the inlet valve and closing the outlet valve. The upstroke of the piston compressed the air in the closed system and collapsed the finger-cot, which expelled its contained blood, closed the inlet valve and forced blood through the

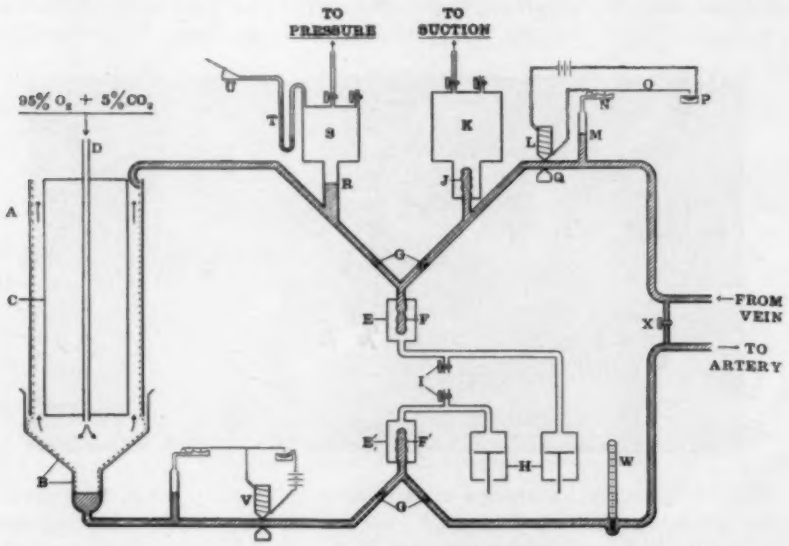

Fig. 2.—Diagram of the apparatus used to withdraw venous blood, introduce oxygen and return the blood to the arterial system. For a description, see the text.

outlet valve. A side arm closed by a needle valve (*I*) projected from the tubing between the air pump (*H*) and the blood pump (*E*). By adjusting this needle valve (*I*), varying degrees of leakage to and from the closed system could be produced. The amount of air leakage controlled the degree of compression and expansion of the finger-cot and hence governed the volume flow of blood through the pump. The venous blood pump (*E*) and the arterial blood pump (*E'*) were similar in all respects. The air piston pumps were driven by a one-quarter horsepower electric motor. The motor was geared by means of pulleys to the piston pumps, so that the latter made 150 complete up and down strokes per minute. This approximates the rate of a cat's heart under barbital anesthesia.

9. de Burgh Daly, I.: A Seven Horse-Power Austin Engine Adapted as a Blood Pump, J. Physiol. **77**:xxxvi, 1933.

10. Dale, H. H., and Schuster, E. H. J.: Double Perfusion Pump, J. Physiol. **64**:356, 1928.

One of the early difficulties encountered was to obtain a rapid free flow of venous blood through the cannula in the jugular vein without sucking the thin wall of the vena cava into the tip of the cannula and so occluding it. When this occurred it produced an immediate cessation of flow and often resulted in the death of the animal. The difficulty was overcome by two means. The first consisted of converting the intermittent flow produced by the pump into a continuous one. By so doing, almost double the flow of blood could be obtained without increasing

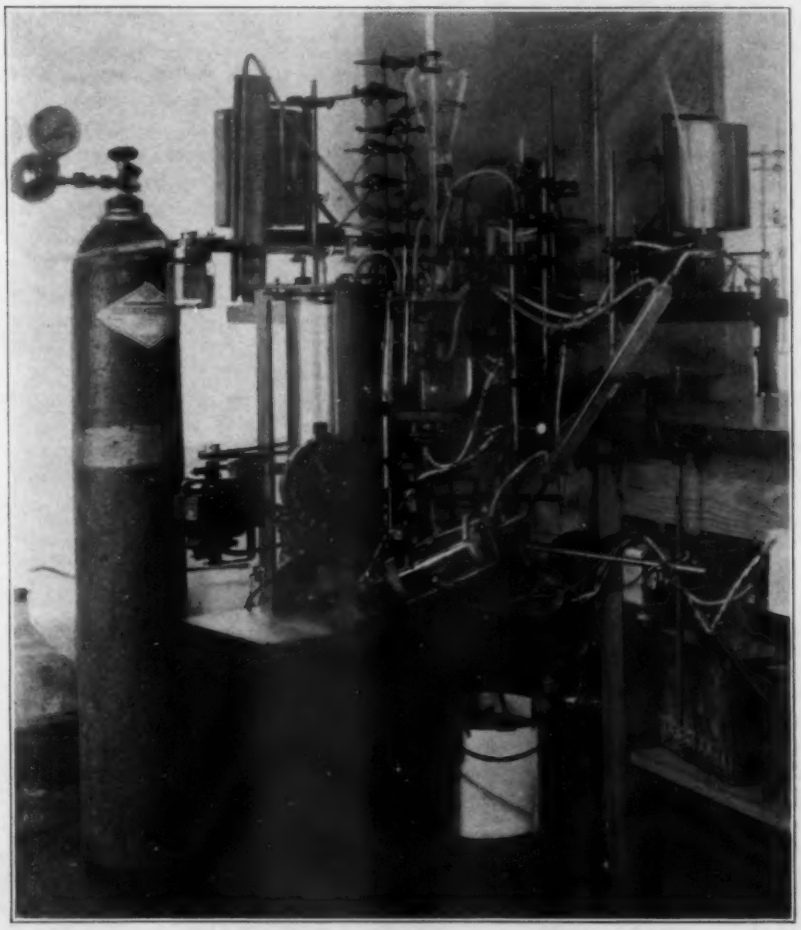

Fig. 3.—Photograph of the apparatus used. The vertical revolving cylinder of the oxygenator can be seen just to the left of the center.

the suction developed by the piston pump; conversely, the same volume output of the venous blood pump could be obtained with approximately one-half the velocity of the blood flow at the tip of the venous cannula. This decrease in the velocity of the flow through the venous cannula diminished the tendency of the wall of the vein to be sucked into the tip of the cannula. The conversion to a smooth flow was accomplished by connecting a rubber finger-cot (*J*) to the side arm of a Y tube inserted in the blood circuit between the inlet blood valve and the venous

cannula. The finger-cot projected into a closed air chamber (*K*) with a capacity of 1,000 cc. in which the air was maintained at a negative pressure just sufficient to expand the finger-cot (*J*) at the end of the expulsion period of the venous blood pump (*E*). With the intake phase of the venous blood pump (*E*), the finger-cot (*J*) partially collapsed, while with the output phase it reexpanded. There was thus maintained a continuous suction of blood through the venous cannula. The rubber finger-cot was used to separate the blood from the air in the chamber (*K*), because direct exposure of the blood to the low partial pressure of oxygen in the air chamber would have resulted in further removal of oxygen from the already venous blood.

The second method of dealing with occlusion of the tip of the cannula by the wall of the vena cava consisted in the use of an automatic magnetic clamp (*LQ*). The action of the clamp was controlled by the following device. A T tube with a vertical side arm (*M*) was placed in the blood circuit, between the magnetic clamp and the venous cannula. The top of the side arm was connected by narrow tubing with a small membrane manometer (*N*). The lever (*O*) of the manometer carried a wire which was bent at its end just above an insulated cup containing mercury (*P*). Contact of the tip of the manometer lever (*O*) with the mercury (*P*) completed a circuit through an electromagnet (*L*). This drew up the bar (*Q*), which compressed the tubing and thus prevented further suction by the venous blood pump. If the tubing between the vertical T tube (*M*) and the venous cannula was occluded by pressure with the fingers while the pump (*E*) was operating, or if the wall of the vein were drawn into the opening of the venous cannula, there occurred a sharp lowering of the meniscus in the vertical T tube and an increase in the negative pressure of the closed air system leading to the membrane manometer. The manometer lever was in consequence drawn down, closing the electrical circuit to the magnetic clamp and thus shutting off the suction of the blood pump from the venous cannula. With the suction cut off, the wall of the vein fell away from the tip of the cannula. Blood would again flow into the cannula and raise the meniscus in the T tube, thus raising the lever (*O*), breaking the electric circuit and allowing suction to begin again.

When the magnetic clamp began to act it was an indication that blood was being withdrawn too rapidly from the superior vena cava. Consequently, the air needle valve (*I*) controlling the flow of blood through the venous blood pump (*E*) was opened slightly to reduce the flow of blood. The magnetic clamp thus served two purposes. It prevented sudden, complete and relatively permanent occlusion of the cannula by the wall of the vein, and it also was an indication of how rapidly blood could be withdrawn from the superior vena cava.

Difficulty was encountered at first in constructing satisfactory valves (*G*) for the blood pumps. The flap valves described by Dale and Schuster[10] could not be adapted to the small lumen of the tubing used. Satisfactory valves which could be used for months without deterioration or leakage were made by cutting four fifths of the way through the small end of a rubber cork at right angles to the long axis of the cork. The flap thus made was from 1 to 2 mm. thick. The edges of the flap were then slightly tapered. The flap was turned back, and a hole was bored through the center of the rubber cork to accommodate a glass tube, which extended to a point just beneath the flap. This provided a valve which had a quick action and did not leak.

A pulsatile flow of blood into the oxygenator produced foaming and splattering. Therefore, a second air chamber was introduced to convert the pulsatile flow into a smooth one. A Y tube with one branch (*R*) in a vertical position was placed in the blood circuit between the pump (*E*) and the oxygenator. The vertical

branch communicated with an air chamber (*S*) with a capacity of 500 cc. in which the air was maintained at a positive pressure. Blood was forced up into the vertical branch of this Y tube with every stroke of the pump. When the stroke was completed, the blood was forced down again by the pressure of the air in the chamber. By this means a practically smooth flow into the oxygenator was obtained.

The pressure in the air chamber (*S*) was recorded by a water manometer (*T*). The pressure readings gave some indication of the volume flow of blood through the venous blood pump because the resistance offered by the tubing between the tube (*R*) and the oxygenator was a constant factor. This was true only if the viscosity of the blood was constant and if the blood level in the tube (*R*) was maintained at a constant level with varying rates of flow by adjusting the pressure in the air chamber (*S*). In several experiments the excursions of this water manometer were recorded on the kymographic record by a small Brodie[11] bellows (*U*) connected to the manometer. The tracing was used merely as an indication of whether the flow through the artificial circuit was increasing or decreasing at any particular moment.

After the blood was exposed to oxygen on the inner surface of the revolving cylinder (*A*), it collected in the cup (*B*). From here it was withdrawn by the arterial blood pump (*E'*). Unless constant attention was paid to the output of the arterial blood pump, the blood level would either rise or fall in the cup (*B*) because of slight differences in the output of the two pumps (*E* and *E'*). Both occurrences were undesirable. If the blood rose in the cup, the volume of blood in the animal's own vessels was reduced. On the other hand, if the level fell to the bottom of the cup, bubbles of oxygen were drawn into the rubber tubing and pumped into the animal's arterial circulation with resultant gas embolism. Both these undesirable consequences were obviated by the use of a second automatic magnetic clamp (*V*), which operated on the same principle as the one previously described. A T tube was inserted between the cup (*B*) and the magnetic clamp (*V*). The top of the T tube was connected to the air chamber of a membrane manometer, the lever of which made and broke an electrical circuit operating the magnetic clamp. When the blood rose in the vertical side arm of the T tube, the circuit was broken and the magnetic clamp was opened. When the level fell, the arm of the manometer was depressed, the electrical circuit was closed and the magnetic clamp was shut. By this method the blood in the cup was prevented from falling below the desired level. The arterial blood pump (*E'*) was always operated at a larger volume rate of flow than the venous blood pump (*E*). This tended to make the level of blood in the cup fall. The fall was continuously checked by the magnetic clamp (*V*). The combination of driving the arterial blood pump at a larger volume flow than the venous pump, plus the constant checking of the magnetic clamp, maintained the level of the blood in the cup within a range of 1 cm.

The importance of maintaining the pulse pressure in the perfusion of organs has been pointed out by numerous investigators.[12] Hence a pulsatile flow through the arterial cannula was thought to be desirable. However, it was found that the pulse pressure produced by the pump was too large and also that the requisite amount of blood could not be forced through the arterial cannula with a com-

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11. Brodie, T. G.: On Recording Variations in Volume by Air-Transmission: A New Form of Volume Recorder, J. Physiol. **27**:473, 1902.

12. Hooker, D. R.: A Study of the Isolated Kidney: The Influence of Pulse Pressure upon Renal Function, Am. J. Physiol. **27**:24, 1910. Gesell, R. A.: On the Relations of Pulse Pressure to Renal Secretion, ibid. **32**:70, 1913.

pletely intermittent flow. Consequently, a short section of wider, more elastic, rubber tubing was placed in the blood circuit between the outlet valve of the arterial blood pump and the arterial cannula. This resulted in a continuous flow with pulsatile increments, and the required amount of blood was easily injected through the arterial cannula.

Rough estimates of the flow of blood through the artificial circuit were made by timing the collection of 10 cc. of blood in the cup at the bottom of the oxygenator. Two horizontal marks were scratched on the lower glass portion of the cup (*B*), so that the volume contained between these marks was 10 cc. During the course of an experiment the level of blood was brought to the lower mark by cutting out the lower magnetic clamp and partially compressing the tubing with the fingers. The tubing was then completely occluded with the fingers until the level reached the upper mark, when the tubing was released and the automatic clamp started again. The time required for the level of blood to rise from the lower to the upper mark was measured with a stop-watch. Even when the lowest value obtained on three or four trials was used, the estimated flow was approximately 10 per cent under the actual flow (measured by collecting the fluid output of the arterial pump). Consequently, the estimates for the flow of blood made during the experiments are probably all slightly low.

The original pumps and tubing held 65 cc. apiece, and their output was only 300 cc. of water per minute. The output of blood was always less than the output of water because of its higher viscosity and greater frictional resistance. As the total blood volume of the cats on which the experiments were performed generally lay between 150 and 300 cc. (computing the volume as 70 cc. per kilogram of body weight), it was desirable to reduce the amount of fluid contained in the pumps and tubing. As finally perfected, the venous blood pump with all its tubing and connections, including the venous cannula, held only 21 cc. of fluid at any moment and was able to deliver 653 cc. of water per minute. The arterial blood pump with all its tubing and connections, including the arterial cannula, held only 20 cc. of fluid and was able to deliver 741 cc. per minute. At the larger rates of blood flow, the oxygenator held 35 cc. of blood on the sides of the revolving cylinder and flat surfaces of the cup. In addition, it was necessary to maintain a small reservoir of 15 cc. in the glass cup at the bottom of the oxygenator. Thus, the pumps, tubing and oxygenator contained a total volume of approximately 90 cc. of fluid while operating at a volume flow of from 300 to 500 cc. of blood per minute.

As the average cat weighing 3 Kg. has a volume of blood of only 210 cc., it was obviously impossible to withdraw enough blood (90 cc.) from the experimental animal to fill the pumps and oxygenator without producing a fatal depletion of blood in the animal's own vessels. Nor was it desirable to fill the pumps and oxygenator with salt solution, as this would rapidly leave the animal's blood vessels when injected into the femoral artery. Consequently, the apparatus was filled with 6 per cent solution of acacia in physiologic solution of sodium chloride. Then when blood was withdrawn from the superior vena cava the solution of acacia was simultaneously injected into the femoral artery, so that the volume of fluid in the animal's own vessels remained constant. The red cells in the average cat would be reduced theoretically by this procedure to roughly two thirds of their previous concentration. This anemia was avoided in a few experiments by the use of heparinized blood from another cat instead of the solution of acacia.

As much of the apparatus as possible was surrounded by a water bath through which water was constantly circulated at a rate of 1,500 cc. per minute by a

small rotary water pump. The water bath circulation has been omitted from figure 2 for the sake of simplicity. The venous blood pump and adjacent portions of the blood circuit were surrounded by water in an inverted bell jar (fig. 3). It was not possible to surround the moving parts of the oxygenator with water. The lower portion of the stationary cup at the bottom of the oxygenator was made of glass and sealed to the upper metal portion (fig. 3). The glass portion had a double wall. Water was circulated through the jacket between the inner and the outer wall. The arterial pump was also surrounded by water. In addition, a 40 cm. condenser jacket enveloped the tubing leading from the outlet valve of the arterial blood pump to the arterial cannula. The temperature of the water was controlled by two electric heating units, placed in a water reservoir with a capacity of 10 liters. The water in this reservoir was constantly circulated through the baths by the water pump. The temperature of the blood entering the femoral artery was recorded by a thermometer (fig. 2 *W*) inserted in the tubing between the end of the condenser jacket and the arterial cannula. With the water bath maintained at approximately 42 C., the temperature of the blood as it entered the arterial cannula could be maintained constantly between 37 and 38 C. The rectal temperature of the animal was usually between 0.2 and 0.3 C. below the temperature of the blood entering the arterial cannula. The temperature of the water bath had to be maintained about 4 C. above the temperature of the blood because of the short exposure of the blood to the heating surfaces after it left the oxygenator in which most of the cooling occurred.

In order to maintain the acacia solution in the pumps and tubing at an even temperature, it was kept in circulation by the pumps during the operative preparation of the animal. This continuous circulation through the oxygenator and pumps was accomplished by opening the short circuit (fig. 2 *X*) and closing the tubing leading to the arterial and venous cannulas. The oxygenator was warmed by the circulating acacia solution to a temperature above that of the room. Thus the cooling and heating factors were stabilized before blood entered the artificial circuit. To start the artificial circulation of the animal it was only necessary to open the tubing leading to each cannula and to close the short circuit.

METHOD

The experiments were performed on cats anesthetized by the intraperitoneal injection of a 10 per cent solution of sodium barbital, 0.45 Gm. per kilogram of body weight. In a few of the later experiments intratracheal ether was used. The blood pressure in the left carotid artery was recorded on a kymograph in the usual manner with a mercury manometer. The obstruction to flow of blood produced by a massive pulmonary embolus was simulated by compressing the pulmonary artery with a clamp. It was essential to have the animal breathing naturally in order to observe the effect of the experimental procedures on the respiration. Therefore, the pulmonary artery was exposed in the earlier experiments by using the heart preparation described by Drinker.[13] A portion of the sternum was removed, and the pericardium was incised from the base to the apex of the heart. The cut edges of the pericardium were sutured to the opening in the wall of the chest. The operative procedure entailed opening both pleural cavities and hence required the use of artificial respiration. When the preparation was completed, artificial respiration was discontinued, and the heart and pulmonary artery were exposed in a naturally breathing animal. In the majority

13. Drinker, C. K.: A Useful Heart Method, J. Exper. Med. **33**:675, 1921.

of experiments a modification of Dinker's technic was used, which did not entail such a large incision or the cross cutting of as much tissue. Through an incision over the left fourth rib, the pectoralis major muscle was split in the direction of its fibers, the pectoralis minor muscle was divided and the left fourth costal cartilage and adjacent rib were removed subperiosteally. The left pleural cavity was opened through the bed of the cartilage and rib. A small transverse opening was made in the pericardium over the pulmonary artery, and the cut edges of the pericardium were sutured to the wall of the chest. This procedure involved less trauma and gave a better exposure of the pulmonary artery than that described by Drinker. A clamp (fig. 9) capable of very fine adjustments was used to compress the pulmonary artery.[14] It was placed and held fixed in position about the pulmonary artery after the preparation of the chest was complete. The percentage of occlusion of the pulmonary artery produced by the clamp could be computed at any point during the compression of the artery.[7]

The right femoral artery was exposed through a small incision, and a cannula filled with saline solution was inserted in a central direction. The right jugular vein was exposed near the base of the neck, and a silver plated metal cannula with a blunt tip was passed into the vein in the direction of the heart for a distance of about 6 cm. The cannula was then firmly held by a clamp in the position in which it most naturally lay without tension. The clamp had two universal joints, which permitted changing the position and direction of the cannula during the experiment if so desired. Glass venous cannulas were used in some experiments, but they were not as satisfactory as the metal cannula because of their fragility. Autopsies were performed at the conclusion of every experiment, and the position of the tip of the venous cannula was noted. It was found to lie in the superior vena cava at varying positions between the junction of the innominate veins and the right auricle. In some experiments the respiratory movements were recorded by means of a fine silk thread connecting the skin of the anterior abdominal wall to a lever which wrote on the kymographic record.

During the preliminary operative procedures the temperature of the animal was maintained by a heating pad placed on the animal board. During the passage of blood through the artificial circuit the body temperature could be maintained by controlling the temperature of the water bath surrounding the artificial circuit. After the operative procedures were completed, heparin was injected intravenously in an amount sufficient to render the blood incoagulable. The preparation of heparin that was used contained 5 units[15] per milligram, and the dose generally employed was 60 mg. per kilogram of body weight. A second, smaller, dose, 40 mg. per kilogram of body weight, was given an hour later. Thereafter it was usually unnecessary to inject more heparin, unless the observations were continued for two or three hours longer. In the majority of experiments a sample of blood was withdrawn at the time that the heparin was injected, and a hematocrit reading was made, Wintrobe's technic being used.[16] At the conclusion of the experiment a second sample of blood was withdrawn, and another hematocrit reading was made. The supernatant plasma in the hematocrit tube was examined

14. Gibbon, J. H., Jr., and Churchill, E. D.: The Mechanical Influence of the Pericardium upon Cardiac Function, J. Clin. Investigation **10**:405, 1931.

15. Charles, A. F., and Scott, D. A.: Studies on Heparin: I. The Preparation of Heparin, J. Biol. Chem. **102**:425, 1933.

16. Wintrobe, M. J.: A Simple and Accurate Hematocrit, J. Lab. & Clin. Med. **15**:287, 1929.

for hemolysis. The degree of hemolysis was estimated by comparing the plasma with a Tallqvist hemoglobin scale. This gave a rough indication of the degree of hemolysis for comparison in different experiments.

OBSERVATIONS

Partial Occlusion of the Pulmonary Artery.—In the preliminary experiments the pulmonary artery was compressed until the blood pressure was lowered. The artificial circulation was then begun in an attempt to restore the blood pressure to its original level. Figure 4 is a portion of the kymographic record made during one of these experiments. Section 1 is a record of the blood pressure after the operative procedures had been completed and before the artificial circulation was started. At this time the pumps were circulating the solution of acacia through the oxygenator and across the short-circuiting tubing between the arterial and the venous cannulas. In the fifteen minute period between section 1 and section 2 the solution of acacia was mixed with the blood of the cat by closing the short circuit and opening the tubing to the arterial and venous cannulas. Blood was thus withdrawn from the vena cava, and the solution of acacia was injected into the femoral artery. The artificial circulation was continued for eleven minutes with the pumps running at a small volume output. The tubes leading to the cannulas were then clipped, and the short circuit was opened again. The solution of acacia was thus mixed with the animal's blood prior to the occlusion of the pulmonary artery. This was done so that the effects of the acute anemia thus produced could be observed apart from the effects of occluding the pulmonary artery and starting and stopping the artificial circulation. This experiment was performed before the volume of the fluid contained in the pumps had been reduced. At this time the pumps and oxygenator contained 180 cc., and although the cat was large (5.4 Kg.) the anemia produced by mixing this volume of acacia solution with the animal's blood must have been considerable. No hematocrit readings were made in this experiment, but an increase in the respiratory rate can be observed in the respiratory variations of the blood pressure at the beginning of section 2.

In the second section, during *A*, the pulmonary artery was gradually compressed until it was 71 per cent occluded. This produced a fall in blood presure to a level incompatible with life, and respiration ceased. At *B* the artificial circulation was started, as can be seen in the upper tracing *F*. At *C*, a minute and a half later, respiration began again. At *D* the artificial circulation was stopped, as shown in the upper tracing *F*. The blood pressure subsequently fell, and respiration again ceased. At *E* the artificial circulation was started. The blood pressure then rose, and respiration was resumed at *G*. Thus in this experiment, with a partial

occlusion of the pulmonary artery, the artificial transportation of blood from the venous to the arterial system with the introduction of oxygen was essential to life.

Complete Occlusion of the Pulmonary Artery.—In twenty-one experiments the blood pressure was maintained at an adequate level, and the animal continued to breathe and the heart to beat while the pulmonary artery was completely closed for periods varying from fifteen minutes to two hours and fifty minutes. Figure 5 is a kymographic tracing made in one of these experiments. The first section illustrates the effect on the blood pressure of gradual occlusion (*A*) of the pulmonary artery before the solution of acacia in the pumps was mixed with the animal's blood. The occlusion of the artery was complete at *B*. Respiration had ceased, and the blood pressure had fallen to zero. At *C* the pulmonary

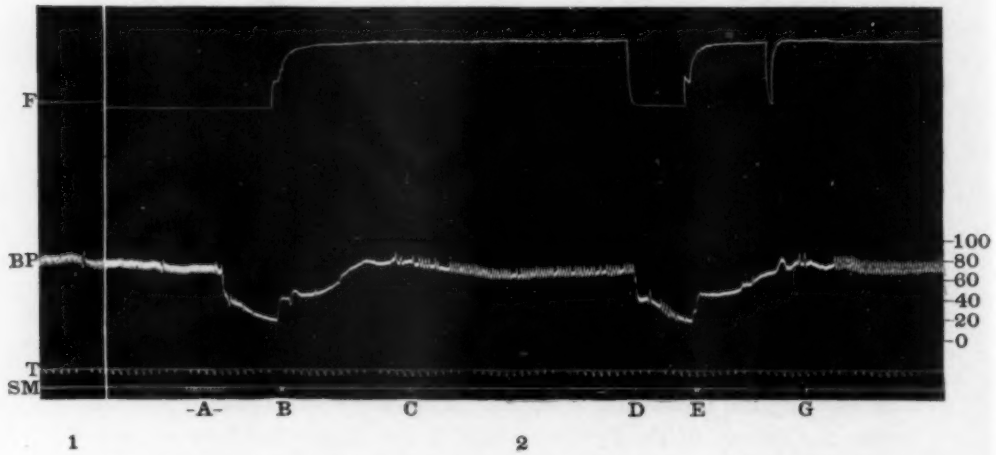

Fig. 4.—Kymographic tracing illustrating the effect on the blood pressure of partial occlusion of the pulmonary artery without and with the artificial circulation of blood. *F* is the pressure in the air chamber *S*, shown in figure 2. Elevation of the tracing indicates a greater flow of blood through the artificial circuit. *B P* is the pressure in the left carotid artery in millimeters of mercury; *T*, the time in five second intervals, and *SM*, the signal magnet tracing. For an explanation of *A* to *G*, inclusive, see the text.

artery was completely released, respiration was resumed and the blood pressure rose to its previous level. The solution of acacia in the artificial circulation was then mixed with the animal's blood by closing the short circuit and opening the tubing to the cannulas. The pulmonary artery was gradually compressed while a small amount of blood was flowing through the artificial circuit. As the compression of the pulmonary artery progressed, the volume of blood pumped through the artificial circuit was increased. The second section of figure 5 shows the terminal stages of compression (*D*) of the pulmonary artery. The

occlusion of the pulmonary artery was complete at *E*. It can be seen that the blood pressure was maintained at a level compatible with life and that the respiratory movements were regular but deeper than before, with an occasional deep sighing breath. Complete occlusion was continued for sixteen minutes in this experiment. During this time the blood pressure remained at the level shown, and the respirations continued to be regular but deep.

Figure 6 is an illustration of a high blood pressure maintained during complete occlusion of the pulmonary artery. Section 1 is a record of the blood pressure and respiration before the blood was mixed with the solution of acacia in the pumps. The second section shows the terminal stages of compression (*A*) of the pulmonary artery while blood was passing through the artificial circuit. The occlusion was

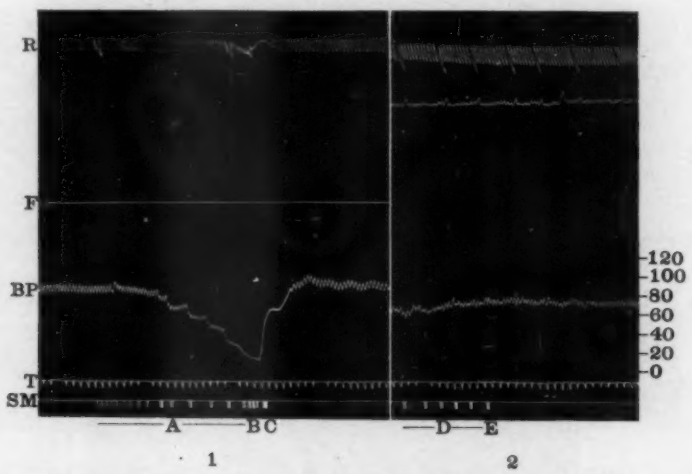

Fig. 5.—Kymographic tracing illustrating the effect on the blood pressure of complete occlusion of the pulmonary artery without and with the artificial circulation of blood. *R* is a tracing of the respirations. *F, BP, T* and *SM* are the same as in figure 4. For an explanation of *A* to *E*, inclusive, see the text.

complete at *B*. The third section was made during the tenth minute of complete occlusion of the pulmonary artery. The blood pressure was 110 mm. of mercury, and the respiratory movements were deep and slow. The pulmonary artery was released nine minutes later because of a break in the water bath circulation surrounding the artificial circuit.

Figure 7 is a record of a more prolonged occlusion. The first section shows the blood pressure and respiration before the blood and the solution of acacia were mixed. The second section shows the terminal stages of compression (*A*), which was complete at *B*. The third section is a record of the blood pressure and respiration during the fortieth minute of complete occlusion of the pulmonary artery. The respiratory

movements were slow and deep, and the blood pressure varied between 100 and 140 mm. of mercury. The large variations in blood pressure were due to a lack of sensitivity in the control of the magnetic clamp below the oxygenator (fig. 2*V*). This was corrected in subsequent

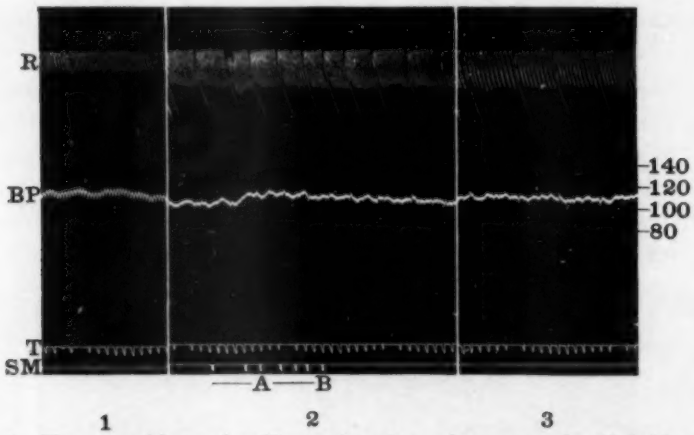

Fig. 6.—Kymographic tracing illustrating the maintenance of a high blood pressure by the artificial circulation of blood during complete occlusion of the pulmonary artery. *R* and *BP* are the same as in figure 5. For a further description, see the text.

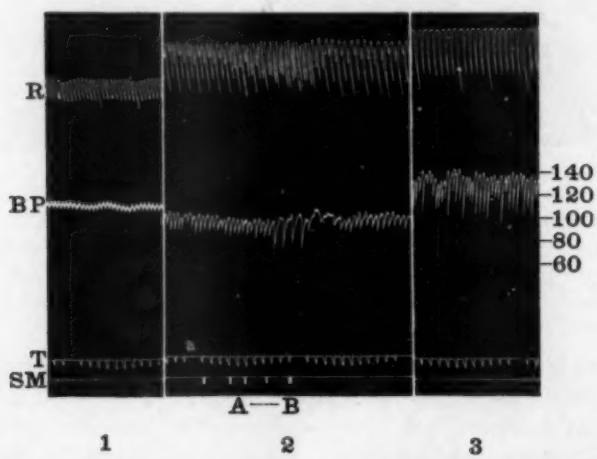

Fig. 7.—Kymographic tracing illustrating the maintenance of the blood pressure and respirations by the artificial circulation of blood during complete occlusion of the pulmonary artery for forty minutes. *R* and *BP* are the same as in figure 5. For a further description, see the text.

experiments, and the pressure swings due to the action of the magnetic clamp were generally less than the normal respiratory variations in blood pressure.

Figure 8 is a kymographic record of the experiment in which the pulmonary artery was completely occluded for the longest period. The first section shows the blood pressure before the blood and solution of acacia were mixed; the second section shows the maintenance of the blood pressure when the pulmonary artery was completely occluded at *A*. The respiratory movements were deep and approximately at the original rate. The third section is the record made during the sixty-eighth minute of complete occlusion of the pulmonary artery. Traube-Hering waves were beginning to appear in the blood pressure, the respiratory rate had become slow and the respiratory movements were not as deep as before. The fourth section was made during the one hundred and twenty-eighth minute of complete occlusion. Traube-Hering waves were marked, and the respiratory rate was still slower.

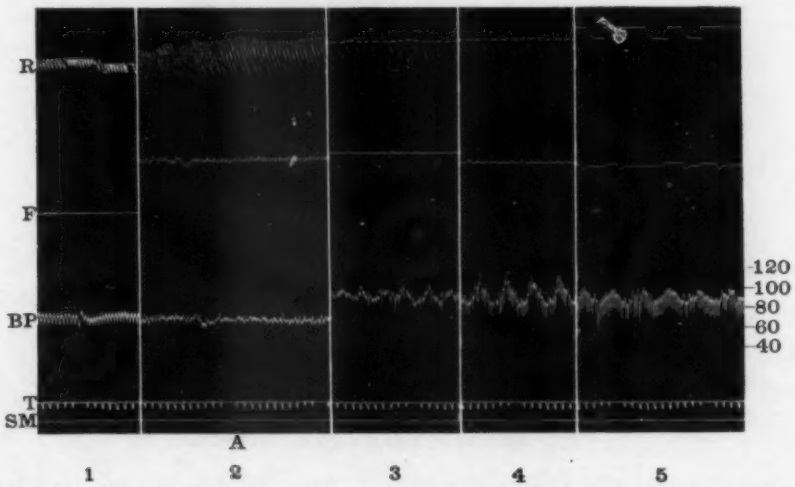

Fig. 8.—Kymographic tracing illustrating the maintenance of the blood pressure and respirations for two hours and thirty-eight minutes with the pulmonary artery completely occluded. *R*, *F* and *BP* are the same as in figure 5. For a further description, see the text.

The fifth section was made during the one hundred and fifty-eighth minute of complete occlusion. The respiratory movements were very slow and irregular. The last breath was taken two hours and fifty-one minutes after the pulmonary artery had been completely occluded.

In these experiments there can be no doubt that the pulmonary artery was completely closed by the clamp. Figure 9 is a drawing of the clamp used. It consists of a tube (*A*), to which the upper jaw of the clamp is fixed. The rod *BC* passes through the tube *A* and is bent to form the lower jaw of the clamp. The upper half of *BC* is wormed and articulates with the knurled nut *D*. An eighth of a turn of the nut moves the

lower jaw of the clamp 0.079 mm. The portion of the rod *BC* bent to form the lower jaw of the clamp is very rigid. The fine worming of the rod *BC* offers an enormous mechanical advantage to the operator moving the knurled nut, and the nut was always tightened firmly when the artery was completely occluded. The jaws of the clamp were of sufficient length to extend beyond the edge of the flattened compressed artery. Furthermore, both the artery and the jaws of the clamp were always under direct vision, so that by no possibility could an unoccluded portion of the artery project beyond the extremities of the jaws. Finally,

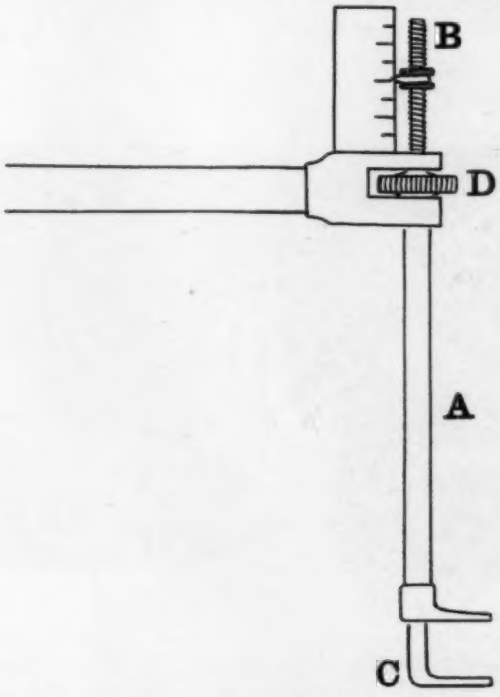

Fig. 9.—Drawing of the clamp used for compression of the pulmonary artery. For a description, see the text.

in the excised heart with the artery compressed by the clamp the pressure in the right ventricle could be raised to 240 mm. of mercury without any fluid being forced through the compressed pulmonary artery. At such a pressure the wall of the right ventricle was distended almost to the point of rupture, and this pressure was obviously many times higher than any that could be developed during life.

Recovery After Complete Occlusion of the Pulmonary Artery.—In a few experiments an attempt was made to study the capacity of the animal to recover spontaneously after a period of complete occlusion

of the pulmonary artery. In three experiments with complete occlusion of the pulmonary artery for thirty, thirty-three and thirty-nine minutes, respectively, the animals were observed for more than two hours after the release of the pulmonary artery and cessation of the artificial circulation. Figure 10 is the kymographic record made in one of these experiments. Section 1 shows the respirations and blood pressure before mixing the solution of acacia and the blood. The indication of flow (*F*) appears on the record because the solution of acacia was being circulated through the pumps and oxygenator. The second section shows the blood pressure during the thirtieth minute of complete occlusion of the pulmonary artery. At this time the flow of blood through the artificial

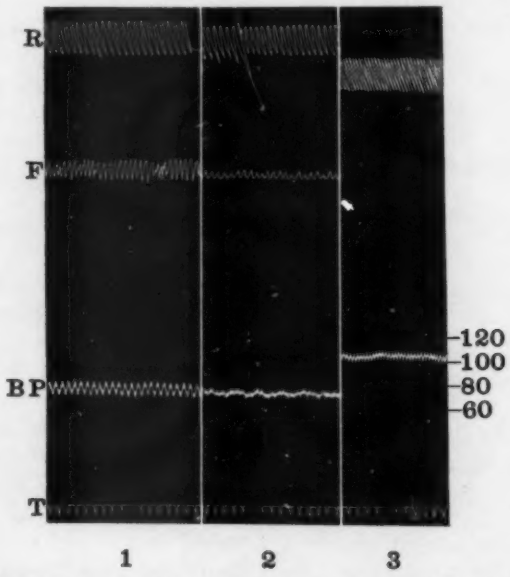

Fig. 10.—Kymographic tracing illustrating the natural maintenance of the blood pressure two and one-half hours after a thirty-nine minute period of complete occlusion of the pulmonary artery. *R*, *F* and *BP* are the same as in figure 5. For a further description, see the text.

circuit was estimated to be 300 cc. per minute. The pulmonary artery was released nine minutes later. The third section is a record of the blood pressure and respiration two and a half hours after the pulmonary artery had been released and the artificial circulation stopped. As can be seen, the blood pressure was maintained at an adequate level by the animal's own heart, and the respiration movements, although deep and rapid, were quite regular. In this experiment, after the artificial circulation had been stopped, the mixture of blood and solution of acacia remaining in the pumps and oxygenator was removed, and some of it

was centrifugated to concentrate the red cells. Eighteen cubic centimeters of the mixture of blood and the solution of acacia and 18 cc. of this concentrated suspension of red cells were returned to the animal's circulation. Even so, the hematocrit reading, taken immediately after this record when the experiment was terminated, showed only 27 per cent cells.

The protocol of the foregoing experiment (30 A) follows. The experiment was performed on May 10, 1935, on a cat weighing 2.86 Kg.

Time	Temp. of Water Bath, C.	Temp. of Fluid in Artificial Circuit, C.	Rectal Temp., C.	Notes
A. M.				
9:52				12.8 cc. of a 10 per cent solution of sodium barbital injected into peritoneal cavity
11:29				Tracheotomy performed; cannula tied into trachea; Drinker heart preparation started
11:52				Artificial respiration begun
P. M.				
12:23			36.8	Artificial respiration stopped; Drinker heart preparation completed
1:07			38.0	
1:17				Right jugular vein and right femoral artery exposed
1:40				While clamp was put around pulmonary artery, right side of heart became distended and blue and respirations ceased; clamp removed and artificial respiration started
1:43				Heart recovered normal tone; artificial respiration stopped; cat breathing normally
1:50	39.4	31.0	37.2	Circulation of solution of acacia by pumps through shunt started; oxygenator started; heating pad turned to "low"
1:58				Clamp in place about pulmonary artery
2:05				175 mg. of heparin (60 mg. per kilogram of body weight) in 8.5 cc. of saline solution injected intravenously; hematocrit sample no. 1 taken
2:10	41.3	36.5	37.0	
2:33				Cannula in jugular vein
2:40	42.8	38.7	37.2	Cannulas in femoral and carotid arteries
2:55	41.2	36.7	37.4	Heating pad turned off
3:02	40.2	36.8	37.6	

Time	Temp. of Water Bath, C.	Temp. of Fluid in Artificial Circuit, C.	Rectal Temp., C.	Notes
3:03				Flow of 95% oxygen 5% carbon dioxide started into oxygenator at rate of 5 liters per minute
3:04	40.0	36.7	37.5	
3:07				Shunt closed and tubing to arterial and venous cannulas opened, starting artificial circulation
3:09	40.8	37.2	37.4	
3:12				Compression of pulmonary artery begun; five turns of knurled nut on clamp (17% occlusion)
3:13				Three full turns and three half turns of nut (66% occlusion)
3:15	40.7	36.3	37.1	
3:16				Four quarter turns of nut (83% occlusion)
3:18				Rate of revolution of oxygenator increased
3:20	41.0	36.6	36.8	One quarter turn of nut (87% occlusion); color of arterial blood bright red now
3:22				Three quarter turns of nut; pulmonary artery completely occluded; arterial blood bright red
3:23				Rate of revolution of oxygenator reduced, because of tendency of blood to foam at faster rate
3:24	41.3	36.8	36.8	
3:28				160 mg. of heparin given intravenously
3:30	42.0	36.8	36.8	Right ventricle moderately distended; heart rate is synchronous with blood pump
3:32				Oxygenator rate, 467 revolutions per minute; moderately deep respirations
3:34				Blood flow through artificial circuit timed; 10 cc. in 2.3, 2.9, 2.2 and 2 seconds; blood flow about 300 cc. per minute
3:37	42.4	37.1	36.8	
3:41	42.6	37.3	36.8	
3:45	42.2	37.1	36.8	
3:49	42.2	37.2	36.8	
3:52	42.3	37.3	36.8	
3:55				5 cc. of acacia solution added to blood in artificial circuit
3:56	42.7	37.3	36.8	
4:00				Oxygenator rate increased to 519 revolutions per minute; no frothing; arterial blood a good red

Time	Temp. of Water Bath, C.	Temp. of Fluid in Artificial Circuit, C.	Rectal Temp., C.	Notes
4:01				Venous cannula broken; clamp compressing pulmonary artery widely opened; artificial circulation stopped
4:05				Broken cannula removed and jugular vein ligated
4:09			36.4	Heating pad turned to "high"
4:15			36.5	
4:21			37.2	A little bloody fluid from artificial circuit injected into femoral artery; heating pad turned to "low"
4:31			37.8	Heating pad turned off
4:43			37.8	
4:48			37.7	
4:59			37.2	9 cc. of bloody fluid from artificial circuit injected into the femoral vein; heating pad turned to "medium"
5:01			37.2	Heating pad turned to "low"
5:28				9 cc. of same fluid injected into the right femoral vein
5:29			37.3	
5:40			37.4	Heating pad turned off
5:45			37.4	Slight Traube-Hering waves in blood pressure tracing; heating pad turned to "low"
5:50				8 cc. of sedimented red blood cells injected into femoral vein
6:00			37.3	Traube-Hering waves almost imperceptible
6:14				5 cc. of sedimented red blood cells injected into femoral vein
6:15			37.4	
6:25			37.3	
6:27				5 cc. of sedimented red blood cells injected into femoral vein
6:30			37.3	Traube-Hering waves present
6:33				Traube-Hering waves gone
6:36				Hematrocrit sample no. 2 taken from femoral artery
6:43				Animal killed

Hematocrit sample no. 1 (before artificial circulation), 50 per cent cells.

Hematocrit sample no. 2, no hemolysis of plasma; 27 per cent cells.

Autopsy.—There was a small hematoma in the superior mediastinum. Both lungs were expanded and pink and floated in water. There were no purpuric spots on the surface of the lungs or on cross-section. Microscopic examination of a section of the lower lobe of the right lung showed a few minute areas of atelectasis.

There was no pulmonary edema. The heart was normal in appearance externally and on cross-section, except for an ecchymotic spot about 1 cm. in diameter on the anterior surface of the heart overlying the interventricular septum near the base. One coronary artery lay directly in the middle of this area. The artery was opened for a distance of 2 cm. No embolus was present. On cross-section this area appeared to be a subepicardial hemorrhage and did not extend into the myocardium. A section of the left ventricular wall through this area was examined microscopically. There was a small hemorrhage beneath the epicardium and in the very superficial portion of the myocardium about the coronary artery and its accompanying veins. There was no embolism or thrombosis of the vessels. No fragmentation or evidence of injury to cardiac muscle fibers was seen.

Experiments with Sterile Technic.—To discover whether the passage of blood through the artificial circuit produced any injurious after-effects on an animal, the following experiment was performed under sterile conditions in order to permit a prolonged survival period. Seventy per cent alcohol was circulated through the pumps, tubing and oxygenator for thirty minutes. The pumps and oxygenator were then thoroughly rinsed with 4 liters of sterile physiologic solution of sodium chloride and filled with a sterile solution of acacia. A small catheter was introduced into the trachea through the mouth, and anesthesia was maintained by ether vapor through the catheter. The chest was not opened. The right jugular vein and femoral artery were exposed through small incisions, and cannulas were introduced in the usual manner. Seventy-two milligrams of heparin per kilogram of body weight was given intravenously. The cannulas were then connected with the artificial circuit, and blood was withdrawn from the jugular vein and reinjected into the femoral artery, at a rate varying from 150 to 200 cc. per minute. Passage of blood through the artificial circuit at this rate was continued for one hour, after which the cannulas were removed and the vessels ligated. The wounds were then sutured. A sample of blood withdrawn at the end of the experiment contained 28 per cent cells and showed slight hemolysis. Recovery was uneventful except for the development of hematoma in both wounds. Five days later there was evidence of infection in the wounds, and the animal was killed. Blood obtained at autopsy was not hemolyzed, and no organisms were grown on culture. Thus it is possible to operate on an animal and render the blood incoagulable by the administration of heparin without causing a fatal hemorrhage from the operative wounds. The experiment also demonstrated that an animal can live for five days after its blood has been passed through the artificial circuit for a period of an hour.

Several attempts were made under sterile conditions to perform the entire experimental procedure of occluding the pulmonary artery, maintaining life by artificial circulation and then releasing the pulmonary artery and allowing the animal to recover. Fifteen such attempts were made unsuccessfully. In addition to the difficulties encountered in per-

forming the experiments under aseptic conditions, two other major complicating factors were present. One was the fact that the procedure was too long and too shocking to be entirely completed in one stage, so that in the majority of these fifteen experiments a preliminary operation was performed. The fourth rib and costal cartilage were resected, the pericardium was opened over the pulmonary artery and the cut edges of the pericardium were sutured to the pectoralis minor and intercostal muscles about the opening in the wall of the chest. The pectoralis major muscle and the skin were then closed over the pulmonary artery. After an interval of about two weeks the experiments were performed as has been described. The old incision was reopened, and the pulmonary artery was immediately exposed beneath the pectoralis major muscle. Occasionally infection prevented the performance of the second stage. At other times a dense plaque of scar tissue was found overlying the pulmonary artery, adherent to it and to the opening in the wall of the chest. In these instances an adequate exposure of the pulmonary artery could be obtained only by a tedious, time-consuming and hazardous dissection.

The other major difficulty encountered was that of anesthesia. Sodium barbital (0.45 Gm. per kilogram of body weight) injected intraperitoneally in the nonsterile experiments always produced prolonged narcosis and a lowering of the blood pressure. Both these effects were undesirable in the sterile survival experiments. Reduction of the amount of barbital resulted in inadequate surgical anesthesia. For these reasons ether was used in the sterile experiments, as it did not lower the blood pressure and the cats recovered consciousness a short time after the inhalation of ether vapor was stopped. The use of an inhalation anesthetic increased the difficulties of the experimental procedure because anesthesia could not be maintained in the ordinary manner when the pulmonary artery was completely occluded. While the pulmonary artery was occluded, ether vapor was circulated through the oxygenator in order to maintain anesthesia. The following technic was employed: During the operative procedures anesthesia was maintained by ether entering the lungs through an intratracheal catheter passed between the vocal cords with the aid of a laryngoscope. As the pulmonary artery was gradually occluded by the clamp, the amount of ether vapor entering the tracheal catheter was reduced, and ether vapor was added in increasing amounts to the oxygen and carbon dioxide mixture entering the oxygenator. Finally, the administration of ether by the intratracheal catheter was discontinued entirely, and anesthesia was maintained by ether vapor in the oxygenator. When the pulmonary artery was released, the reverse procedure was carried out. This double administration of ether required the undivided attention of one person throughout the experiment.

That the entire procedure can be successfully carried through with the animal under ether anesthesia was shown by experiment 64. This experiment was not sterile, but the technic was otherwise similar to that used in the sterile experiments, and ether anesthesia was employed throughout. The pulmonary artery was completely occluded for thirty minutes, during which time life was maintained by the artificial circulation. The artificial circulation was continued at a reduced volume flow for fifty-three minutes after the pulmonary artery was released. It was then stopped. The cannulas were removed from the femoral artery and the jugular vein. These vessels were ligated, and the wounds were closed. The wound in the chest was also closed after the clamp was removed from the pulmonary artery. The animal died two hours after the artificial circulation was stopped. The respiratory rate became increasingly rapid before death. Autopsy showed bilateral pneumothorax and practically complete collapse of both lungs. However, the animal apparently recovered consciousness after the ether anesthesia was stopped. All four limbs and the head were moved, and the animal made several attempts to stand up.

COMMENT

There are several features of the apparatus and method which could be improved on. For example, all the experiments were performed in the presence of marked acute anemia. Hematocrit readings were made at the conclusion of twenty-seven experiments. The percentage of cells varied between 4 and 29, the median value being 13.5 per cent. This anemia resulted from dilution of the animal's blood with the solution of acacia in the artificial circuit. The dilution was avoided in a few experiments by filling the pumps and tubing with blood from one or more cats. The dilution might also be diminished by further reducing the fluid capacity of the pumps, tubing and oxygenator. During the course of these experiments the volume of the pumps and tubing was reduced from an initial 130 cc. to a final 41 cc. Any further reduction in volume would entail a relatively large increase in the velocity of the blood with an increase in trauma and hemolysis. However, the volume of fluid required in the pumps and tubing could probably be reduced by simplification in design. It is not possible to make any significant reduction in the volume of blood required in the oxygenator. Here again a different design might accomplish the purpose. The success obtained despite the severe anemia seems to indicate that the circulation might be maintained with relative ease if the anemia were avoided, provided the blood was still adequately oxygenated.

There was some difficulty in avoiding hemolysis. At times this was due to inadequate rinsing of the pumps and oxygenator with physio-

logic solution of sodium chloride. In twenty-six experiments the degree of hemolysis was noted. It varied from none to 40 per cent. The latter figure refers to the color on a Tallqvist hemoglobin scale to which the color of the plasma most nearly compared. The hemolysis of 40 per cent occurred immediately after a marked reduction in size of the glass and rubber tubing composing the artificial circuit. It was reduced to less than 10 per cent by the use of larger tubing where the flow of blood was most rapid, that is, between the blood valves of each pump where the flow was completely intermittent. Avoidance of sharp changes in direction of the blood stream was also thought to decrease trauma and hemolysis.

Heparin was used as an anticoagulant. A dose sufficient to render all the blood incoagulable was given. In one experiment (described previously) in which the animal survived for five days, a single dose of 350 mg. of heparin was given to a cat weighing 4.9 Kg. Gross [17] has shown that heparin given intravenously produces an immediate increase in clotting time. The rate of return to normal is rapid at first and then slower. He noted that the effect of heparin in rabbits tended to vary directly with the dose. In one experiment 10 mg. of heparin was injected in a rabbit weighing 1.7 Kg. A return to the normal clotting time began in twenty minutes and was complete in one and a half hours. Howell [18] has shown that when enough heparin has been used to make all of an animal's blood incoagulable the coagulation time returns to normal in three hours. In a dog weighing 13½ pounds (6 Kg.), enough heparin to render the blood incoagulable was injected daily for six days, without noticeable effect on the red or white cells, platelet count or clotting time twenty-four hours after each injection.[19] With a purified preparation of heparin, ten transfusions of blood have been given in man, with slight reactions in two instances.[18]

In twenty-one experiments the pulmonary artery was completely occluded for fifteen minutes or more. In only one of these experiments was the occlusion maintained for more than an hour. In this instance respirations continued for two hours and fifty-one minutes with the pulmonary artery completely occluded. In all the other experiments it was possible to maintain the occlusion of the pulmonary artery for only an hour or less. A frequent cause of failure to maintain the occlusion for longer periods was some defect in the apparatus. In the others, however, a gradual decrease occurred in the amount of venous blood

17. Gross, P.: Duration of Anticoagulant Action of Heparin in Vivo in Relation to Dosage, Proc. Soc. Exper. Biol. & Med. **26**:383, 1929.

18. Howell, W. H.: The Purification of Heparin and Its Chemical and Physiological Reactions, Bull. Johns Hopkins Hosp. **42**:199, 1928.

19. Howell, W. H., and McDonald, C. H.: Note on the Effect of Repeated Intravascular Injections of Heparin, Bull. Johns Hopkins Hosp. **46**:365, 1930.

which could be withdrawn without sucking the venous wall into the tip of the cannula. This probably indicated a decreased venous return to the heart, which was not due to a failure of respiration because the respiratory movements were almost invariably deeper than normal. It may have been due to the gradual loss of fluid from the blood into the tissues. This seems a likely explanation, although the blood pressure was generally maintained above the level which is associated with the development of shock. The increased depth of the respiratory movements would seem to indicate an insufficient supply of oxygen to both the capillaries and the tissues. Lack of oxygen increases permeability of the capillaries,[20] and this in turn might account for loss of fluid from the blood. In most experiments there was probably an adequate saturation of the arterial blood with oxygen, but there was always a severe acute anemia, and the volume flow of blood may not have been adequate to compensate for this. The reversal of the flow of blood in the abdominal and the thoracic aorta may have been a contributing factor, because the branches now formed acute angles with the direction of the flow of blood instead of angles between 90 and 180 degrees. From simple principles of hydraulics, this would result in a diminished flow of blood through these branches. This argument would apply to the abdominal viscera but not to the branches on the arch of the aorta supplying the head and upper extremities. However, no hemorrhages or edema were observed at autopsy in the abdominal viscera on gross examination. Finally, there is another possible cause of the gradually diminishing venous return. There is a possibility that very minute bubbles of oxygen were drawn into the lower arterial blood pump and then physically dissolved in the plasma by the high pressure developed in the tubing leading to the arterial cannula. With a return to the lower pressure in the animal's vessels the bubbles of oxygen might reform and thus block the systemic capillaries.

There was undoubtedly an excessive loss of water vapor from the blood during its passage through the oxygenator. In the experiment in which the occlusion was maintained for two hours and fifty minutes, the mixture of oxygen and carbon dioxide was warmed to 37 C. and saturated with water vapor before being passed through the oxygenator. The water vapor, however, condensed on the cool copper tube leading through the stationary cylinder of the oxygenator and dripped into the blood. There was excessive hemolysis in this experiment which must have been partly due to this factor. The rate of condensation under similar conditions was determined the following day. Water was found

20. Landis, E. M.: Micro-Injection Studies on Capillary Permeability: III. The Effect of Lack of Oxygen on the Permeability of the Capillary Wall to Fluid and to the Plasma Proteins, Am. J. Physiol. **83**:528, 1928.

to drip from the copper tube at the rate of 23 cc. an hour. As blood passed through the artificial circuit for over three hours, more than 70 cc. of water must have been introduced into the circulation by this means. No further attempts were made to saturate the gas entering the oxygenator with water vapor, although this probably should have been done and the condensation avoided by warming the metal tube.

Various types of apparatus have been designed for perfusion of isolated organs and even whole animals. So far as I am aware there has been no report of a successful temporary substitution of an entirely mechanical apparatus for the heart and lungs of an animal. Lindbergh [21] has described an apparatus for the prolonged sterile perfusion of isolated organs. Gibbs [22] has devised an artificial heart for use in cats and dogs which has proved helpful in the investigation of pharmacologic problems.[23] The artificial heart is connected to the great vessels within the pericardium, and the blood is oxygenated in the animal's own lungs. Barcroft [24] carried out successful perfusion of a dog by tying cannulas in the aorta and great veins and circulating the blood by means of a centrifuge pump. The blood was oxygenated by passing it through a heart lung preparation of another dog.

None of these methods could be employed in the solution of our problem. Our object was to determine whether the circulation could be temporarily aided by mechanical means in the presence of an obstruction of the pulmonary artery. This temporary mechanical aid was necessarily of such nature as not to interfere with the ultimate survival of the animal. The withdrawal and reinjection of blood had to be accomplished through peripheral vessels of such size that the loss of their continuity by ligation would entail no serious ultimate consequences.

SUMMARY

The object of these experiments was to determine whether the circulation could be aided by artificial means in the presence of partial or complete occlusion of the pulmonary artery. The means employed were the withdrawal of blood from a peripheral vein, the introduction of oxygen into that blood and the reinjection of the blood into a peripheral artery in a central direction. The blood was thus short circuited around the obstruction in the pulmonary artery, and a part or all of the work

21. Lindbergh, C. A.: An Apparatus for the Culture of Whole Organs, J. Exper. Med. **62**:409, 1935.

22. Gibbs, O. S.: An Artificial Heart, J. Pharmacol. & Exper. Therap. **38**: 197, 1930; Artificial Heart for Dogs, ibid. **49**:181, 1933.

23. Tainter, M. L.: Use of the Gibbs Artificial Heart in the Study of Circulatory Phenomena, Arch. internat. de pharmacodyn. et de thérap. **42**:186, 1931.

24. Barcroft, H.: Observations on the Pumping Action of the Heart, J. Physiol. **78**:186, 1933.

of the heart and lungs was temporarily taken over by artificial means. This mechanical aid to the circulation in the presence of a partial or complete occlusion of the pulmonary artery has been satisfactorily demonstrated. Because of the necessity for employing a sterile technic, the ability of an animal to recover for more than a few hours from complete occlusion of the pulmonary artery has not been demonstrated. Further improvement and simplification of the apparatus and technic are probably necessary before successful results with a sterile technic can be obtained.

CONCLUSIONS

1. Short circuiting blood around a partial obstruction in the pulmonary artery by means of a perfusion apparatus aids in maintaining the blood pressure and respiration.

2. Life can be maintained for short periods of time in the presence of complete obstruction of the pulmonary artery by a perfusion method which does not involve damage to the great vessels of the body.

3. The normal circulation and respiration can be spontaneously reestablished and maintained for several hours after a thirty minute period of complete occlusion of the pulmonary artery.

EFFECT OF VAGOTOMY ON THE GASTRIC MOTOR MECHANISM OF MAN

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The influence of the vagus nerve on the gastric motor mechanism has inspired extensive investigation; nevertheless, diversity of opinion concerning its precise effect on the human stomach still exists. As a result, vague and paradoxical functions have been suggested. Apparent discrepancies are due in part to the infrequency of direct observations on man. These, however, are being gradually eliminated through the recent controlled investigations of human gastric function.

The wider recognition of indications for indirect or physiologic surgical treatment has increased the number of opportunities for the study of the neurogenic control of human function. During recent years attempts have been made to ameliorate certain abnormal states by the extirpation of organs related physiologically to the nature of the fundamental disease. Although these surgical procedures have been instituted primarily for their therapeutic effect, nevertheless, they have provided opportunities for the investigation of the physiologic properties of these organs. Thus, bilateral resection of the splanchnic nerves for the relief of juvenile diabetes [1] made possible observations on one phase of the nervous control of the human stomach. The results of our own studies in this field have already been reported.[2]

Presented before the Forty-Eighth Annual Meeting of the American Physiological Society, Washington, D. C., March 26, 1936.

From the Department of Surgery, Yale University School of Medicine and the Department of Medical and Surgical Research, Ohio State University.

1. de Takáts, Géza, and Fenn, G. K.: Bilateral Splanchnic Nerve Section in a Juvenile Diabetic, Ann. Int. Med. **7**:422 (Oct.) 1933. de Takáts, Géza; Fenn, G. K., and Trump, Ruth A.: Splanchnic Nerve Section in Juvenile Diabetes, ibid. **7**:1201 (April) 1934.

2. Barron, Louis E.; Curtis, George M., and Haverfield, William T.: The Effect of Bilateral Resection of the Splanchnic Nerves on Gastric Motility in Man, Arch. Surg. **32**:577 (April) 1936.

A further analysis of the effect of the extrinsic innervation on the gastric motor mechanism of man became possible when abdominal vagotomy was accomplished in the course of the management of a patient with vagotonia, a symptom complex described by Eppinger and Hess.[3] In addition to the usual clinical studies, observations were made on the motor activities of the stomach before and after resection of the left abdominal vagus nerve and also during the therapeutic administration of atropine. The purpose of this paper is to report these results.

The present investigation was made possible through the cooperation of Dr. Bruce K. Wiseman, of the Medical Division of the Department of Medical and Surgical Research, Ohio State University. The diagnosis was made by him after a thorough investigation for more than a year.[4] During this period various medical measures were employed in an attempt to control the condition. It was found that large doses of atropine produced definite symptomatic relief. Untoward by-effects of this treatment, however, were pronounced, and vagotomy was finally advised in an effort to relieve permanently the abdominal distress and attendant symptomatology. The preliminary and subsequent studies have demonstrated that many symptoms were the result of perverted physiologic gastro-intestinal activities. The clinical syndrome of vagotonia with the medical management pertaining to this patient is to be reported elsewhere by Dr. Wiseman.

HISTORICAL BACKGROUND

Because of certain physiologic implications, surgical interference with the extrinsic nerve supply to the human stomach has been advised and accomplished since 1899 for many organic and functional gastric abnormalities. Jaboulay[5] was one of the first to extirpate the celiac plexus. Exner[6] performed subdiaphragmatic resection of the vagus nerve in the management of tabetic crises. Postoperatively he observed gastric dilatation, atony and pylorospasm. Because of this he proposed gastrostomy or gastrojejunostomy.

Bircher[7] performed vagotomy for the control of ulcer. He reported a subsequent disappearance of many distressing epigastric symptoms, associated with a reduction in the gastric secretion and acidity. In the

3. Eppinger, H., and Hess, L.: Vagotonia, Nervous and Mental Disease Monograph 20, New York, Nervous and Mental Disease Publishing Company, 1917.

4. Wiseman, Bruce K.: Personal communication to the authors.

5. Jaboulay: Zentralbl. f. Chir. **28**:227, 1901; cited by McCrea.[13]

6. Exner, A.: Tabische Krisen, Ulcus ventriculi und Vagus, Wien. klin. Wchnschr. **25**:1405, 1912. Exner, A., and Schwarzman, E.: Gastrische Krisen und Vagotomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **28**:15, 1914.

7. Bircher: Arch. d. mal. de l'app. digestif **11**:135, 1921; cited by McCrea.[13]

management of certain gastric disorders, Latarjet [8] recommended resection of all the extrinsic nerves in order to decrease the frequency and intensity of the gastric contractions. He reported that this operation was most suitable for patients with vagotonia in whom there was no gastric lesion.

The importance of the nervous element in the etiology of gastroduodenal ulcer was emphasized by Schiassi.[9] He concluded that rest to the stomach and duodenum was of paramount importance and that this could be accomplished by gastroduodenal denervation, supplemented, if necessary, by gastro-enterostomy. Schiassi's operation was virtually a circumcision in the pyloric region. He reported excellent results.

Other investigators were less optimistic. Steinthal [10] performed vagotomy on two patients with gastric ulcer and reported that the motility of the stomach was not influenced. He maintained that this operative procedure was ineffective in influencing ulcers situated high on the lesser curvature. Borchers [11] did not recommend section of the vagus nerve in order to influence reflex spasm and hypermotility because he did not regard the vagus as a true motor nerve. Best and Orator [12] advised against section of the nerve for the treatment of peptic ulcer.

McCrea [13] and Laignel-Lavastine [14] presented a more favorable outlook for this procedure. McCrea pointed out that organic stricture of the esophagus was one of the chief contraindications. Stenosis of the pylorus could be benefited most by other surgical procedures. Another more theoretical contraindication is that after gastric denervation visceral sensation may be abolished. In the absence of this protective mechanism, a serious lesion such as carcinoma of the stomach may develop silently. An analogous syndrome has been reported by Latarjet.[8]

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8. Latarjet, A.: Résection des nerfs de l'estomac: Technique opératoire; résultats cliniques, Bull. Acad. de méd., Paris **87**:681, 1922. Latarjet, A., and Wertheimer, P.: Denervation of the Stomach, Presse méd. **31**:993, 1923.

9. Schiassi, Benedetto: The Rôle of the Pyloro-Duodenal Nerve Supply in the Surgery of Duodenal Ulcer, Ann. Surg. **81**:939, 1925.

10. Steinthal, C.: Blocking of the Sympathetic and Vagus Nerves, Zentralbl. f. Chir. **47**:1293, 1920; cited by McCrea.[13]

11. Borchers, E.: Motilitätsstörungen des Magens und Vagus Resektion, Zentralbl. f. Chir. **47**:1535, 1920.

12. Best, Russel R., and Orator, Victor: The Vagus Nerve and Its Relation to Peptic Ulcer, Ann. Surg. **96**:184, 1932.

13. McCrea, E. D.: The Nerves of the Stomach and Their Relation to Surgery, Brit. J. Surg. **13**:621, 1925.

14. Laignel-Lavastine: L'étude du sympathique et son intérêt chirurgical, Rev. de chir. **62**:663, 1924.

SURGICAL ANATOMY

Detailed descriptions of the anatomic relationship between the vagus nerve and the stomach have been published elsewhere.[15] In brief, the nerve passes from the neck into the thorax and to the esophagus, there forming the so-called esophageal plexus (fig. 1). From this there arise two main trunks, an anterior and a posterior trunk (fig. 2). The anterior trunk passes downward through the diaphragm along the lesser curvature of the stomach. McCrea[15] reported that the pylorus is innervated by the hepatic branch of the anterior trunk of the vagus

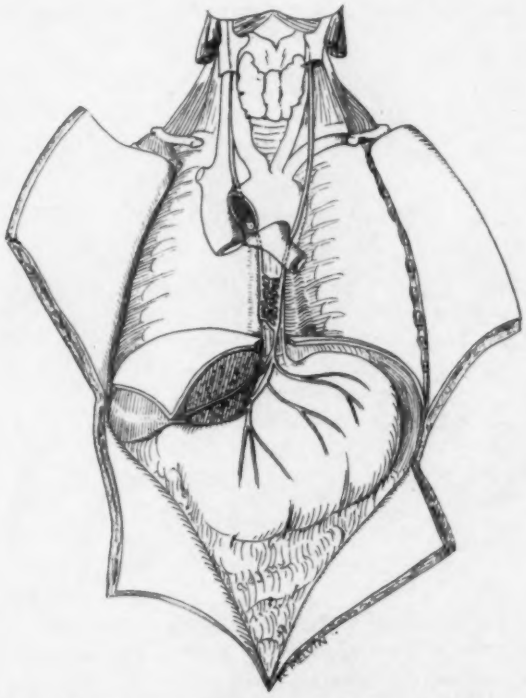

Fig. 1.—Drawing from an anatomic preparation showing the formation of the esophageal plexus.

nerve. The posterior trunk sends branches to the posterior surface of the stomach and to the pancreas, spleen, kidneys and small intestine.

Prior to vagotomy dissections were made in the anatomic laboratory in order to ascertain the relationship of the vagus nerve to the stomach and the neighboring viscera. Anterior (left) abdominal vagotomy was then accomplished on May 7, 1935, on our patient. The previous anatomic studies revealed that the best surgical approach to this nerve in the

15. (*a*) McCrea, E. D.: The Abdominal Distribution of the Vagus, J. Anat. **59**:18, 1924. (*b*) McCrea.[13]

region of the cardia was through a high left rectus-splitting incision (fig. 3, insert). A thorough exploration at the time of the operation revealed the spleen, kidneys, adrenals, liver, gallbladder and large intestine to be normal. Complete examination of the stomach failed to disclose evidence of demonstrable disease. The stomach was then retracted downward, thus making the anterior trunk of the vagus nerve prominent to palpation (fig. 3). The nerve was identified and carefully dissected downward from the diaphragm to the cardia and along the lesser curvature. Care was taken not to injure the left gastric artery, which was in close proximity. A segment of the vagus nerve, about 3 cm., was then resected with its branches along the cardia. Because of the obvious

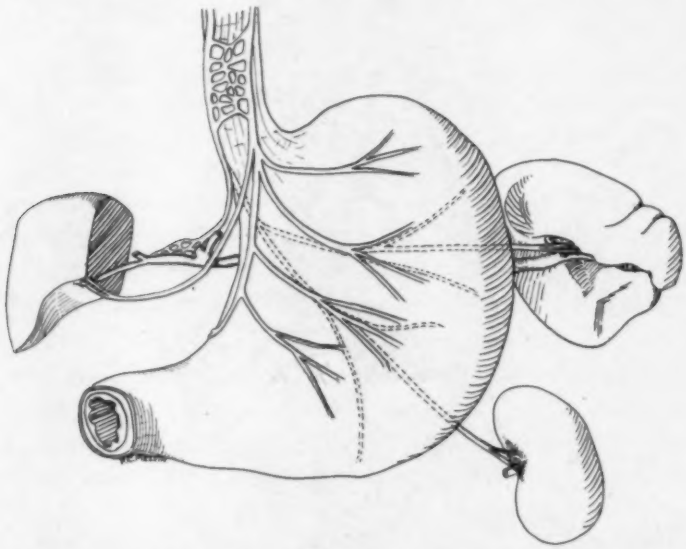

Fig. 2.—Drawing from an anatomic preparation showing the origin of the anterior and posterior trunks of the vagus nerve and their relationship to the stomach and the neighboring viscera.

anatomic difficulty in adequately exposing the posterior trunk of the nerve and because this branch of the nerve is considered to be of lesser physiologic significance,[16] it did not seem prudent to subject the patient to the additional trauma necessitated by its resection. The wound was closed in the usual manner. The patient left the operating room in

16. (*a*) Bechterew and Mislawski: Ztschr. f. klin. Med. **29**:73, 1896; cited by McSwiney, B. A.: Innervation of the Stomach, Physiol. Rev. **11**:478, 1931. (*b*) Batelli, F.: Action de diverses substances sur les mouvements de l'estomac et innervation de cet organe, Compt. rend. Acad. d. sc. **122**:1568, 1896. (*c*) May, W. P.: The Innervation of the Sphincters and Musculature of the Stomach, J. Physiol. **31**:260, 1904.

good condition. Contrary to the findings of Exner,[6] we did not observe any evidence of gastric atony or of dilatation occurring as an immediate or remote complication.

METHODS OF INVESTIGATING GASTRIC MOTILITY

The gastric motor mechanism was investigated by the balloon and kymographic method. As a preliminary measure, a balloon coated with barium sulfate and attached to a narrow rubber tube was swallowed. Roentgenologic visualization[2] of the balloon in the stomach made it possible to determine the accurate distance from this position to the incisor teeth. This was 50 cm. The tube was kept in this

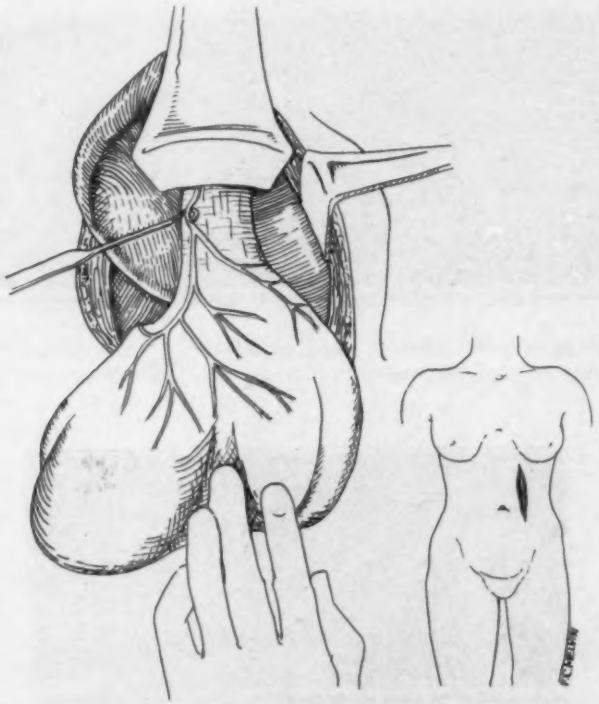

Fig. 3.—Drawing demonstrating the method of isolating the anterior trunk of the vagus nerve. By downward traction on the stomach, the nerve can be identified easily. The insert demonstrates the abdominal incision through which anterior abdominal vagotomy can be best accomplished.

position throughout each observation. Studies were made in the morning, about fourteen hours after the preceding meal. The details concerning the apparatus and the criteria employed in the evaluation of gastric motility have been described in a previous communication.[2]

The usual duration of each period of observation was approximately five hours. Thirteen experiments were made during the control period (table 1). After this the patient was given atropine, the dose of which varied with the character of the symptoms. The average dose was 75 minims (4.6 cc.) daily of the tincture of belladonna. Occasionally it was necessary to increase the dose. Nine observations

were made during this medication (table 2). Anterior (left) abdominal vagotomy was then performed. Studies of the gastric motility were resumed about a week later, and twelve subsequent observations were made (table 3). This patient returned to the hospital about five months after vagotomy for reinvestigation. Seven experimental observations were made at that time (table 4).

Accompanying these studies, observations were made on the emptying time of the stomach (table 5). The patient was given a test meal consisting of 3 ounces (93 Gm.) of Cream of Wheat, 2 ounces (62 Gm.) of barium sulfate and sufficient water to form a paste. As soon as the meal was eaten, fluoroscopy was performed to determine the gastric capacity. Fluoroscopic observations were then repeated at frequent intervals until barium was no longer evident in the stomach.

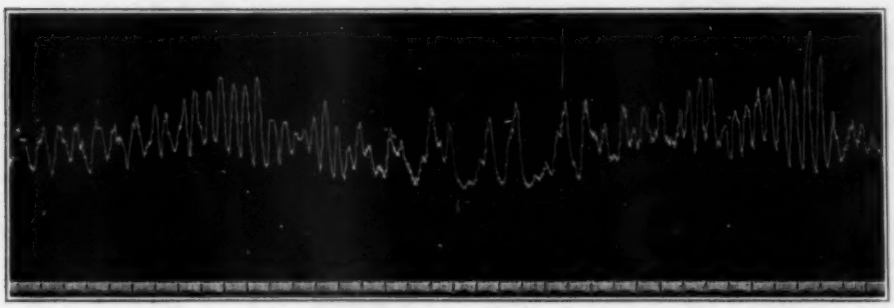

Fig. 4.—Kymographic tracing made on March 4, 1935, showing continuous gastric motility throughout an observation period of five hours and five minutes.

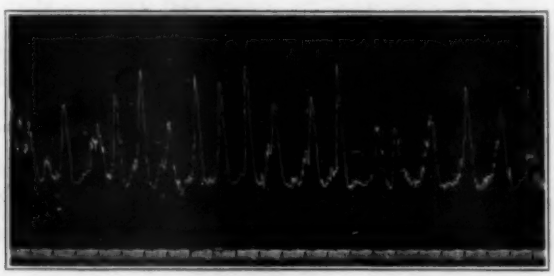

Fig. 5.—Tracing made on Feb. 25, 1935, showing a definite increase in the duration of periods of gastric motility. The total duration of this period was two hundred and sixty-seven minutes.

Attention was directed to the pylorus and to the body of the stomach in order to observe changes in tonus and contractility. Observations were made on the total emptying time, that is, the period from the time the test meal was eaten until it was seen no longer in the stomach. Owing to an occasional persistent coating of the walls of the stomach by barium, it was sometimes difficult to ascertain accurately when the stomach was completely empty, a difficulty also noted by other investigators.[17] This artefact, however, was not constant.

17. McCrea, E. D.; McSwiney, B. A., and Stopford, J. S. B.: The Effect on the Stomach of Section of the Vagi Nerves, Quart. J. Exper. Physiol. **16**:195, 1926.

TABLE I.—*Analysis of Experiments on Gastric Motility During the Control Period* *

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Contractions					Comment
		No.	Duration	No.	Duration	Type	No.	Duration	Interval Between	Amplitude	
2/ 4/35	3 hr. 30 m.	Continuous motility; type I and II contractions; occasional intense contractions									
2/14/35	4 hr. 5 m.	1	34 m.	1	27 m.	I	Inestimable	Inestimable	Inestimable	Low grade	
				1	29 m.	II	28	Max. 50 s. Min. 20 s.	Max. 1 m. Min. 25 s.	Max. 4.5 cm. Min. 1.5 cm.	
		1	31 m.	1	31 m.	I	Inestimable	Inestimable	Inestimable	Low grade	
				1	93 m.	II	79	Max. 45 s. Min. 20 s.	Max. 2 m. Min. 25 s.	Max. 3.5 cm. Min. 2.5 cm.	
2/21/35	5 hr. 15 m.	..	.....	1	74 m. 10 s.	II	46	Max. 1 m. Min. 20 s.	Max. 4 m. 30 s. Min. 40 s.	Max. 4.5 cm. Min. 2 cm.	
		1	52 m. 50 s.	1	43 m. 40 s.	II	35	Max. 45 s. Min. 30 s.	Max. 4 m. 15 s. Min. 5 s.	Max. 4.8 cm. Min. 1 cm.	Period of motility terminated in tetany
		1	103 m. 20 s.	1	26 m. 20 s.	II	20	Max. 50 s. Min. 20 s.	Max. 2 m. 45 s. Min. 25 s.	Max. 4 cm. Min. 1.5 cm.	Occasional contraction during period of quiescence
		1	15 m. 40 s.								
2/24/35	5 hr.	..	.....	1	229 m.	I	Inestimable	Inestimable	Inestimable	Low grade	Occasional severe contraction during this period
				1	49 m.	II	19	Max. 50 s. Min. 15 s.	Max. 7 m. 15 s. Min. 1 m.	Max. 7.5 cm. Min. 1.5 cm.	Patient complained of abdominal distress during this period
		1	22 m.								
2/25/35	5 hr. 35 m.	..	.....	1	48 m.	II	42	Max. 1 m. 10 s. Min. 20 s.	Max. 3 m. 20 s. Min. 10 s.	Max. 3 cm. Min. 1.5 cm.	
		1	20 m.	1	267 m.	II	230	Max. 1 m. 15 s. Min. 10 s.	Max. 2 m. Min. 15 s.	Max. 3.5 cm. Min. 1.5 cm.	Intense gastric motility
2/26/35	6 hr. 15 m.	..	.....	1	38 m.	II	25	Max. 1 m. 10 s. Min. 30 s.	Max. 1 m. 10 s. Min. 20 s.	Max. 4 cm. Min. 1.5 cm.	
		1	54 m.	1	28 m.	II	16	Max. 50 s. Min. 30 s.	Max. 1 m. 35 s. Min. 30 s.	Max. 8 cm. Min. 2 cm.	Intense gastric motility
		1	107 m.	1	41 m.	II	27	Max. 2 m. Min. 20 s.	Max. 1 m. Min. 10 s.	Max. 7.5 cm. Min. 1.5 cm.	
		1	107 m.								
3/ 4/35	5 hr. 5 m.	Continuous motility; type I and II contractions; occasional intense contractions									
3/ 7/35	3 hr.	Continuous low grade motility with fluctuations in gastric tonus									
3/ 8/35	3 hr.	Continuous motility; type I and II contractions									
3/14/35	5 hr.	..	.....	1	42 m.	I	Inestimable	Inestimable	Inestimable	Low grade	
		1	14 m.	1	42 m.	II	33	Max. 1 m. Min. 25 s.	Max. 1 m. 45 s. Min. 10 s.	Max. 4 cm. Min. 2 cm.	Occasional contractions during period of quiescence
		1	98 m.	1	67 m.	II	42	Max. 50 s. Min. 35 s.	Max. 3 m. Min. 15 s.	Max. 3.5 cm. Min. 1.5 cm.	
		1	37 m.								
3/17/35	2 hr. 27 m.	..	.....	1	70 m.	I and II	50	Max. 50 s. Min. 5 s.	Max. 2 m. 30 s. Min. 5 s.	Max. 3 cm. Min. 1 cm.	Period terminated in tetany
		1	49 m.	1	28 m.	I	Inestimable	Inestimable	Inestimable	Low grade	
3/20/35	5 hr.		.....	1	26 m.	II	24	Max. 45 s. Min. 10 s.	Max. 20 s. Min. 5 s.	Max. 3.5 cm. Min. 1.5 cm.	Period terminated in tetany
		1	14 m.	1	53 m.	I and II	Inestimable	Max. 1 m. Min. 20 s.	Max. 1 m. 10 s. Min. 5 s.	Max. 3.5 cm. Min. 1 cm.	
		1	19 m.	1	124 m.	II	57	Max. 1 m. Min. 10 s.	Max. 8 m. Min. 5 s.	Max 4.5 cm. Min. 1.5 cm.	
		1	64 m.			..	..	.....	.....	.....	Patient given 0.4 units of insulin 9 m. after onset of this period; no change in gastric motility
3/21/35	5 hr. 10 m.	..	.....	1	163 m.	Fluctuations in gastric tonus					
				1	30 m.	II	18	Max. 1 m. Min. 30 s.	Max. 2 m. Min. 1 m.	Max. 6.5 cm. Min. 1.5 cm.	
				1	117 m.	II	45	Max. 1 m. Min. 40 s.	Max. 4 m. Min. 1 m.	Max. 3 cm. Min. 1 cm.	Balloon ruptured due to severe contraction; patient given 0.4 units of insulin 43 minutes after onset of period; no change in gastric motility

* In this table and in tables 2, 3 and 4, m. indicates minutes; s., seconds; Min., minimum, and Max., maximum.

Observations on the emptying time of the stomach were made during an adequate control period, during the therapeutic administration of atropine and subsequent to anterior (left) abdominal vagotomy (table 5).

RESULTS WITH BALLOON METHOD

The results obtained during the preoperative control period are recorded in table 1. Intense gastric motility was a common observation. Occasionally this persisted throughout an entire period of observation (fig. 4). When a period of gastric quiescence was observed, it frequently was of short duration. In a few instances there were periods of quiescence lasting over one hundred minutes. However, the average duration of the periods of motility was definitely increased (fig. 5) in contrast to the duration of periods of quiescence.

Occasionally it was impossible to estimate accurately the number of, the duration of, and the interval between, contractions because of the rapidity with which they occurred. In the majority of instances definite objective measurements could be made. These are recorded in table 1.

A signal magnet and an electric key were incorporated into the system. The patient was instructed to indicate any abdominal pain by pressing the key. This made it possible to correlate by kymographic tracings any abdominal discomfort with the associated phase of gastric motility. Such a relationship was observed. During the control period severe contractions were noted, occasionally of sufficient magnitude to rupture the balloon (table 1). These contractions seemed to occur simultaneously with the epigastric distress.

Gastric tetany [2] was common. This too was accompanied by transitory discomfort, which practically always disappeared with the ensuing period of gastric quiescence. With the resumption of intense gastric motility, there was a simultaneous recurrence of epigastric distress.

The duration of periods of quiescence is recorded in table 1. The number of contractions during periods of motility, tabulated here, was definitely increased, probably because of the increase in the duration of periods of gastric motility. The amplitude of the contractions was also increased, occasionally to 7.5 and 8 cm. This too was not constant. Great variability existed. In general, there was a definite increase in gastric tonus as demonstrated by the balloon method.

After the control period the patient was given large doses of atropine, which varied with the symptoms manifested. Nine observations were made. The data are given in table 2.

During this medication the observations revealed a slight reduction in the intensity of the motor activities of the stomach. In many instances the contractions were low. Frequently weak fluctuations in gastric tonus (fig. 6) persisted throughout the period of observation. When tetany appeared, it was feeble and usually not accompanied by epigastric dis-

TABLE 2.—*Analysis of Experiments on Gastric Motility During Medication with Atropine*

TABLE 2.—*Analysis of Experiments on Gastric Motility During Medication with Atropine*

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Contractions					Comment
		No.	Duration	No.	Duration	Type	No.	Duration	Interval Between	Amplitude	
4/17/35	5 hr.	..	.....	1	95 m.	I	Inestimable	Inestimable	Inestimable	Max. 2.5 cm. Min. 1.5 cm.	
		1	62 m.	1	62 m.	I	Inestimable	Inestimable	Inestimable	Max. 2.5 cm. Min. 1.0 cm.	Low grade motility throughout observation period
		1	42 m.	1	29 m.	I	Inestimable	Inestimable	Inestimable	Max. 1.5 cm. Min. 1.0 cm.	
4/20/35	5 hr.	1	38 m.	Low grade motility, duration 262 minutes. Fluctuations in gastric tonus noted							
4/22/35	5 hr. 15 m.	Continuous low grade motility with fluctuations in gastric tonus									
4/25/35	4 hr. 35 m.	1	29 m.	1	45 m.	II	41	Max. 40 s. Min. 10 s.	Max. 55 s. Min. 5 s.	Max. 4 cm. Min. 2 cm.	
		1	63 m.	1	92 m.	II	66	Max. 50 s. Min. 5 s.	Max. 2 m. 20 s. Min. 5 s.	Max. 4.5 cm. Min. 2 cm.	Patient experienced abdominal discomfort synchronous with each contraction
		1	46 m.								
4/27/35	4 hr. 25 m.	..	.....	1	20 m.	I, II and III	Inestimable	Inestimable	Inestimable	Max. 3.5 cm. Min. 1.5 cm.	Period terminated in tetany
		1	18 m.	1	86 m.	I, II and III	Inestimable	Max. 1 m. Min. 5 s.	Max. 2 m. Min. 5 s.	Max. 2.5 cm. Min. 1.5 cm.	Period terminated in tetany
		1	35 m.	1	43 m.	II and III	Inestimable	Max. 1 m. Min. 5 s.	Max. 2 m. 40 s. Min. 5 s.	Max. 2.5 cm. Min. 1.5 cm.	Period terminated in tetany
		1	32 m.	1	31 m.	II	13	Max. 1 m. Min. 30 s.	Max. 2 m. 40 s. Min. 1 m.	Max. 3 cm. Min. 1.5 cm.	
4/30/35	5 hr.	..	.....	1	36 m.	II	31	Max. 50 s. Min. 25 s.	Max. 50 s. Min. 10 s.	Max. 4 cm. Min. 1.5 cm.	
		1	16 m.	1	54 m.	I, II and III	Inestimable	Max. 1 m. 5 s. Min. 15 s.	Max. 1 m. Min. 5 s.	Max. 4 cm. Min. 1.5 cm.	Period terminated in tetany
		1	14 m.	1	118 m.	II	104	Max, 1 m. 5 s. Min. 25 s.	Max. 1 m. 35 s. Min. 10 s.	Max. 3 cm. Min. 2 cm.	Period terminated in tetany
		1	36 m.	1	26 m.	II	13	Max. 1 m. Min. 50 s.	Max. 2 m. Min. 50 s.	Max. 2.5 cm. Min. 2 cm.	
5/ 2/35	5 hr. 23 m.	..	.....	1	64 m.	I	Inestimable	Max. 1 m. 5 s. Min. 5 s.	Max. 2 m. Min. 5 s.	Max. 3.5 cm. Min. 1.5 cm.	
		1	58 m.	1	30 m.	I	Inestimable	Inestimable	Inestimable	Inestimable	Occasional contraction during period of quiescence
		1	64 m.	1	49 m.	II	36	Max. 50 s. Min. 10 s.	Max. 2 m. Min. 5 s.	Max. 3 cm. Min. 1 cm.	
		1	58 m.								
5/ 3/35	5 hr.	..	.....	1	65 m.	I and II	Inestimable	Max. 40 s. Min. 10 s.	Max. 2 m. Min. 10 s.	Max. 3.5 cm. Min. 2 cm.	
		1	42 m.	1	60 m.	I and II	42	Max. 1 m. Min. 10 s.	Max. 1 m. 35 s. Min. 10 s.	Max. 3 cm. Min. 1.5 cm.	
		1	37 m.	1	96 m.	II	76	Max. 1 m. Min. 15 s.	Max. 2 m. 20 s. Min. 10 s.	Max. 3.5 cm. Min. 2 cm.	
5/ 4/35	4 hr.	..	.....	1	55 m.	II	36	Max. 1 m. 40 s. Min. 20 s.	Max. 1 m. 55 s. Min. 10 s.	Max. 4 cm. Min. 2 cm.	Period terminated in tetany
		1	26 m.	1	103 m.	II	70	Max. 1 m. Min. 30 s.	Max. 4 m. 30 s. Min. 10 s.	Max. 4.5 cm. Min. 1.5 cm.	
		1	45 m.	1	11 m.	I	Inestimable	Low grade motility			

tress. Although in some instances the contractions measured from 4 to 5 cm., in general there was a definite decrease in the amplitude. Associated with the slight decrease in gastric tonus, there was a moderate reduction in the number of contractions. The duration of the contractions remained unchanged, but there was a slight increase in the interval between contractions (fig. 7). Some symptomatic relief was experienced during the use of atropine.

After left abdominal vagotomy twelve experiments were made by the balloon method. The results are recorded in table 3. After vagotomy there ensued a definite decrease in the duration of periods of gastric

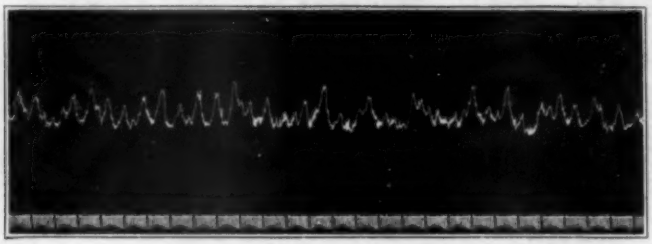

Fig. 6.—Tracing made on April 20, 1935, showing low grade motility with fluctuations in gastric tonus during intense medication with atropine.

Fig. 7.—Tracing made on May 4, 1935, showing an increase in the interval between contractions during intense medication with atropine.

motility (fig. 8). This in turn was associated with a corresponding increase in the duration of periods of quiescence (fig. 9). Frequently the motility was low grade and blended with weak fluctuations in gastric tonus. When contractions were observed, they were feeble (fig. 10).

The various criteria associated with the contractions are recorded in table 3. The number of contractions during each period of motility was decreased. Although the duration of the contractions remained essentially unchanged, there was an increase in the interval between contractions. In some instances this was nine and twelve minutes (fig. 11), in contrast to an approximate average of two minutes during

TABLE 3.—*Analysis of Experiments on Gastric Motility After Anterior (Left) Abdominal Vagotomy*

Date of	Periods of Quiescence	Periods of Activity	Contractions	Comment

TABLE 3.—*Analysis of Experiments on Gastric Motility After Anterior (Left) Abdominal Vagotomy*

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Contractions					Comment
		No.	Duration	No.	Duration	Type	No.	Duration	Interval Between	Amplitude	
5/21/35	5 hr.	..	.....	1	58 m.	II	21	Max. 1 m. 10 s. Min. 40 s.	Max. 4 m. 30 s. Min. 1 m. 30 s.	Max. 4 cm. Min. 2 cm.	Interval between contractions was definitely increased
		1	75 m.	1	107 m.	II	37	Max. 45 s. Min. 30 s.	Max. 12 m. 20 s. Min. 1 m.	Max. 3 cm. Min. 1.5 cm.	Approximate interval between contractions, about 2 m.
		1	60 m.								
5/23/35	5 hr. 30 m.	..	.....	1	43 m.	II	19	Max. 55 s. Min. 30 s.	Max. 3 m. Min. 55 s.	Max. 2.5 cm. Min. 1 cm.	
		1	80 m.	1	63 m.	II	24	Max. 55 s. Min. 30 s.	Max. 4 m. 35 s. Min. 45 s.	Max. 3.5 cm. Min. 1.5 cm.	Average interval between contractions, about 2 m.
		1	65 m.	1	30 m.	II	15	Max. 55 s. Min. 30 s.	Max. 2 m. 35 s. Min. 35 s.	Max. 3 cm. Min. 1.5 cm.	
		1	49 m.								
5/27/35	3 hr. 20 m.	1	27 m.	1	31 m.	II	15	Max. 1 m. Min. 35 s.	Max. 6 m. Min. 40 s.	Max. 4.5 cm. Min. 2 cm.	Occasional contraction during period of quiescence
		1	96 m.	1	46 m.	II	14	Max. 1 m. Min. 40 s.	Max. 7 m. Min. 1 m.	Max. 4.5 cm. Min. 2 cm.	
5/28/35	3 hr.	..	.....	1	24 m.	I and II	Inestimable	Max. 1 m. 15 s. Min. 40 s.	Max. 1 m. Min. 5 s.	Max. 3 cm. Min. 1.5 cm.	
		1	30 m.	1	40 m.	II	32	Max. 1 m. 5 s. Min. 20 s.	Max. 1 m. 35 s. Min. 10 s.	Max. 3 cm. Min. 1.5 cm.	Occasional contraction during period of quiescence
		1	58 m.	1	33 m.	II	21	Max. 1 m. Min. 35 s.	Max. 2 m. 30 s. Min. 1 m.	Max. 2.5 cm. Min. 1.5 cm.	
5/29/35	5 hr.	1	28 m.	1	35 m.	II	19	Max. 1 m. Min. 20 s.	Max. 4 m. Min. 45 s.	Max. 3 cm. Min. 1.5 cm.	
		1	117 m.	..	.....	..	..	.....	.....	.....	Rhythmic tonus changes
5/30/35	3 hr.	..	.....	1	50 m.	II	27	Max. 55 s. Min. 10 s.	Max. 1 m. 30 s. Min. 5 s.	Max. 2.5 cm. Min. 1 cm.	Period terminated in gastric tetany
		1	23 m.	1	107 m.	II	50	Max. 1 m. 10 s. Min. 40 s.	Max. 9 m. Min. 1 m.	Max. 3 cm. Min. 1 cm.	Rhythmic tonus changes noted between contractions
6/24/35	3 hr.	1	30 m.	1	27 m.	II	37	Max. 45 s. Min. 10 s.	Max. 2 m. 40 s. Min. 10 s.	Max. 4.5 cm. Min. 2 cm.	Period ended in weak gastric tetany
		1	123 m.								
6/25/35	Continuous low grade motility throughout the observation period										
6/26/35	3 hr.	..	.....	1	27 m.	II	23	Max. 50 s. Min. 25 s.	Max. 1 m. Min. 15 s.	Max. 4 cm. Min. 2.5 cm.	
		1	63 m.	1	25 m.	II	18	Max. 50 s. Min. 30 s.	Max. 2 m. Min. 5 s.	Max. 7.5 cm. Min. 2 cm.	
		1	49 m.	1	16 m.	II	7	Max. 45 s. Min. 30 s.	Max. 2 m. 15 s. Min. 2 m.	Max. 2 cm. Min. 1 cm.	Motility of low amplitude
6/27/35	3 hr.	..	.....	1	35 m.	II	27	Max. 1 m. Min. 30 s.	Max. 1 m. 10 s. Min. 10 s.	Max. 3.5 cm. Min. 1.5 cm.	
		1	49 m.	1	27 m.	II	25	Max. 45 s. Min. 25 s.	Max. 1 m. Min. 35 s.	Max. 3.5 cm. Min. 1 cm.	
		1	69 m.								
6/28/35	3 hr.	1	17 m.	1	34 m.	II	32	Max. 55 s. Min. 10 s.	Max. 50 s. Min. 10 s.	Max. 3 cm. Min. 1.5 cm.	
		1	27 m.	1	44 m.	I and II	Inestimable	Max. 50 s. Min. 5 s.	Max. 1 m. 30 s. Min. 5 s.	Max. 3 cm. Min. 1 cm.	Occasional contraction during period of quiescence
		1	58 m.								
6/29/35	3 hr. 5 m.	..	.....	1	35 m.	II	30	Max. 1 m. Min. 15 s.	Max. 1 m. 10 s. Min. 10 s.	Max. 3.5 cm. Min. 1.5 cm.	
		1	14 m.	1	56 m.	I and II	Inestimable	Inestimable	Inestimable	Max. 4 cm. Min. 1.5 cm.	
				1	80 m.	I	Inestimable	Inestimable	Inestimable	Low grade	

TABLE 4.—*Analysis of Experiments on Gastric Motility Five Months After Anterior (Left) Abdominal Vagotomy*

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Contractions					Comment
		No.	Duration	No.	Duration	Type	No.	Duration	Interval Between	Amplitude	
9/21/35	3 hr.	1	44 m.	1	23 m.	II	14	Max. 1 m. Min. 10 s.	Max. 3 m. Min. 5 s.	Max. 4 cm. Min. 1.5 cm.	Period terminated in weak tetany
		1	108 m.	1	5 m.	II	5	Max. 35 s. Min. 10 s.	Max. 1 m. Min. 5 s.	Max. 2 cm. Min. 1.5 cm.	
9/23/35	5 hr. 5 m.	..	.....	1	54 m.	II	35	Max. 1 m. Min. 5 s.	Max. 3 m. 10 s. Min. 5 s.	Max. 3 cm. Min. 1.5 cm.	
		1	69 m.	1	24 m.	II	16	Max. 50 s. Min. 5 s.	Max. 4 m. 10 s. Min. 5 s.	Max. 2.5 cm. Min. 1.5 cm.	Low amplitude
		1	42 m.	1	50 m.	II	26	Max. 45 s. Min. 10 s.	Max. 4 m. 10 s. Min. 10 s.	Max. 3 cm. Min. 1 cm.	
		1	66 m.								
9/24/35	5 hr.	..	.....	1	9 m.	II	Inestimable	Inestimable	Inestimable	Low grade	
		1	20 m.	1	39 m.	II	40	Max. 35 s. Min. 5 s.	Max. 25 s. Min. 5 s.	Max. 8 cm. Min. 2.5 cm.	Intense motility
		1	112 m.	1	19 m.	II	20	Max. 15 s. Min. 5 s.	Max. 15 s. Min. 5 s.	Max. 5.5 cm. Min. 2.5 cm.	
		1	58 m.	1	43 m.	II	40	Max. 50 s. Min. 20 s.	Max. 1 m. 20 s. Min. 10 s.	Max. 6.5 cm. Min. 1.5 cm.	
9/26/35	5 hr. 5 m.	..	.....	1	88 m.	II	55	Max. 1 m. 5 s. Min. 15 s.	Max. 3 m. Min. 15 s.	Max. 4 cm. Min. 1 cm.	
		1	17 m.	1	16 m.	II	8	Max. 45 s. Min. 10 s.	Max. 2 m. 50 s. Min. 1 m.	Max. 4.5 cm. Min. 1.5 cm.	
		1	27 m.	1	40 m.	II	31	Max. 50 s. Min. 5 s.	Max. 2 m. Min. 5 s.	Max. 5 cm. Min. 1.5 cm.	Period terminated in weak tetany
		1	72 m.	1	31 m.	II	14	Max. 1 m. Min. 5 s.	Max. 2 m. 25 s. Min. 5 s.	Max. 4.5 cm. Min. 2.5 cm.	
		1	14 m.								
9/27/35	5 hr.	..	.....	1	14 m.	I	Inestimable	Inestimable	Inestimable	Low grade	
		1	17 m.	1	80 m.	1 and II	Inestimable	Inestimable	Inestimable	Max. 4 cm. Min. 1 cm.	Period terminated in weak tetany
		1	96 m.	1	26 m.	II	26	Max. 45 s. Min. 5 s.	Max. 55 s. Min. 5 s.	Max. 3 cm. Min. 1.5 cm.	
		1	54 m.	1	13 m.	II	19	Max. 40 s. Min. 5 s.	Max. 1 m. 40 s. Min. 5 s.	Max. 3 cm. Min. 1.5 cm.	Patient complained of "gas pains"
10/3/35	5 hr.	1	35 m.	1	41 m.	II	25	Max. 55 s. Min. 10 s.	Max. 4 m. Min. 10 s.	Max. 3.5 cm. Min. 1.5 cm.	
		1	95 m.	1	26 m.	II	15	Max. 1 m. Min. 15 s.	Max. 4 m. 30 s. Min. 5 s.	Max. 3.5 cm. Min. 1 cm.	
		1	103 m.								
10/5/35	5 hr.	1	60 m.	1	21 m.	II	16	Max. 45 s. Min. 10 s.	Max. 4 m. 30 s. Min. 10 s.	Max. 3 cm. Min. 1 cm.	Low amplitude
		1	25 m.	1	26 m.	II	14	Max. 40 s. Min. 5 s.	Max. 5 m. Min. 5 s.	Max. 3 cm. Min. 1 cm.	
		1	106 m.	1	40 m.	I	Inestimable	Inestimable	Inestimable	Low grade	
		1	22 m.								

the preoperative control period. Between the contractions low grade fluctuations in gastric tonus were observed. Many contractions were atypical and therefore could not be classified accurately. Some contractions measured 7 cm., but in general the amplitude was decreased.

This patient returned to the University Hospital about five months after left abdominal vagotomy for the investigation of the late results. These are tabulated in table 4. The data revealed that the changes in the gastric motility previously noted after vagotomy had persisted. The duration of periods of motility was still decreased (fig. 12). The gastric tonus remained low, and the duration of periods of quiescence was

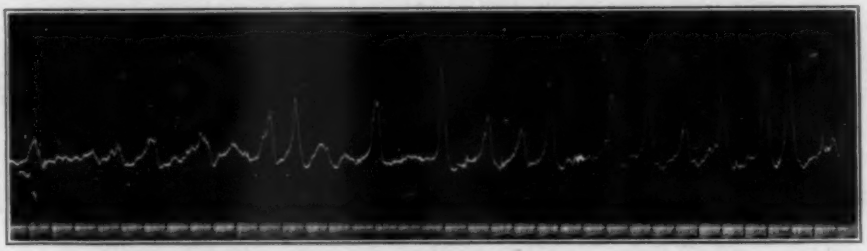

Fig. 8.—Tracing made on May 23, 1935, showing a decrease in the duration of periods of gastric motility after anterior (left) abdominal vagotomy. The total duration of this period was thirty minutes.

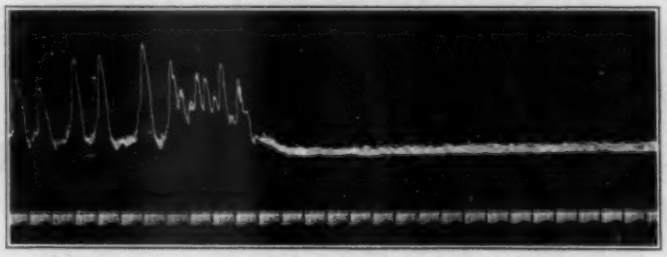

Fig. 9.—Tracing made on May 29, 1935, showing an increase in the duration of periods of gastric quiescence after anterior (left) abdominal vagotomy. The duration of this period was one hundred and seventeen minutes.

increased (fig. 13). The clinical status of the patient, however, was remarkably improved.

THE INFLUENCE OF ATROPINE AND OF VAGOTOMY ON THE EMPTYING TIME OF THE STOMACH

The studies on the total emptying time of the stomach revealed that during the control period there was increased peristaltic activity associated with a delay in the emptying time. This was attributed to spasticity of the pyloric sphincter. Four observations were made. The

results are recorded in table 5. There was some variability. The total emptying time ranged from five hours and thirty minutes to eight hours and averaged six hours and forty-nine minutes. The following is a typical protocol of one observation on the total emptying time made during the control period.

March 6, 1935, 7:30 a. m.: The test meal was eaten at this time.

7:40 a. m.: Except for a small gastric air bubble, the stomach appeared full. Active motility was noted. Deep contractions were observed passing over the stomach. No barium was seen in the duodenum.

8:00 a. m.: There was a slight decrease in the gastric contents. A few flecks of barium were seen in the duodenum. Deep constrictions in the stomach were noted.

9:00 a. m.: The stomach was estimated to be about one-half full. The remainder of the barium was distributed throughout the small intestine. Active peristalsis was observed.

TABLE 5.—*Influence of Atropine and of Anterior (Left) Abdominal Vagotomy on the Emptying Time of the Stomach*

Control Studies	During Medication with Atropine	After Vagotomy
7 hr., 45 min.	5 hr., 15 min.	2 hr., 30 min.
8 hr.	5 hr., 40 min.	2 hr., 45 min.
6 hr.	4 hr., 40 min.	3 hr., 15 min.
5 hr., 30 min.		
Av. 6 hr., 49 min.	Av. 5 hr., 12 min.	Av. 2 hr., 50 min. Five months after vagotomy, 2 hr.

10:15 a. m.: The stomach was estimated at this time to be about one-third full. The gastric contents were in the pyloric portion of the stomach. Considerable barium was seen in the small intestine but none in the large intestine.

11:30 a. m.: There was little change in the quantity of barium in the stomach. Peristalsis at this time was considerably weaker than previously observed.

12:45 p. m.: The stomach was estimated to be less than one-quarter full. The remainder of the barium was in the small intestine. There was active gastric peristalsis. No barium was seen in the large intestine.

2:30 p. m.: The stomach still contained a small amount of barium. The remainder of the barium was in the small intestine.

3:15 p. m.: A small amount of barium was still seen in the stomach; the remainder was in the small intestine.

3:30 p. m.: The stomach now contained no barium. The major portion was seen in the small intestine. Barium was observed in the ascending colon.

The total emptying time was eight hours.

During intense medication with atropine three observations were made (table 5). The results were fairly constant. The emptying time ranged from four hours and forty minutes to five hours and forty minutes and averaged five hours and twelve minutes. It would seem that this decrease in the emptying time of the stomach was due at least in part to a corresponding decrease in the spasticity of the pyloric

sphincter. The following is a typical protocol of an observation made during the medication with atropine.

April 24, 1935, 7:20 a. m.: The test meal was eaten at this time.

7:30 a. m.: The stomach seemed practically full. A few flecks of barium were seen in the duodenum. Active peristalsis was seen passing over the stomach.

8:00 a. m.: The stomach was estimated to be about four-fifths full. The remainder of the barium was in the duodenum. Active gastric peristalsis was observed.

9:00 a. m.: The stomach was estimated to be about one-half full. The remainder of the barium was in the small intestine.

10:00 a. m.: The stomach appeared less than one-half full. Barium was distributed throughout the small intestine.

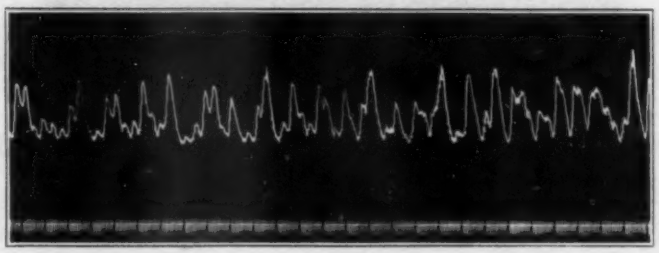

Fig. 10.—Tracing made on May 28, 1935, showing low grade motility after anterior (left) abdominal vagotomy. The duration of this period was forty minutes.

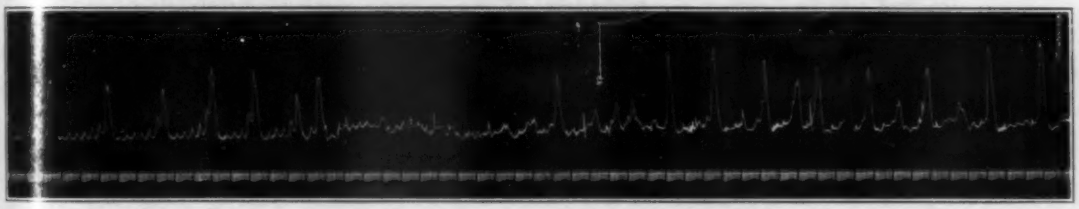

Fig. 11.—Tracing made on May 21, 1935, showing a definite increase in the interval between contractions after anterior (left) abdominal vagotomy. On this day the interval between contractions was increased to twelve minutes and twenty seconds.

11:00 a. m.: The stomach was estimated to be about one-fourth full. The remainder of the barium was distributed throughout the small intestine. No barium was evident in the large intestine.

12:00 m.: The stomach contained a small amount of barium. The remainder of the barium was distributed throughout the small intestine. There was none in the large intestine.

12:30 p. m.: A few flecks of barium were seen in the stomach.

1:00 p. m.: The stomach now contained no barium. It was distributed throughout the small intestine.

The total emptying time was five hours and forty minutes.

After vagotomy the emptying time of the stomach was definitely decreased (table 5). It may seem paradoxical that a relatively hypomotile

stomach as determined by the gastrographic method should evacuate its contents with greater rapidity than during the hypermotile control period. However, in this untreated patient with vagotonia, it would seem that the hypermotility of the stomach was accompanied by marked pylorospasm. This would explain the abnormal retention of the gastric contents.

After left abdominal vagotomy, a patulous pylorus resulted. With each gastric contraction barium was observed passing through the pyloric sphincter, which appeared to be relaxed and relatively atonic, a phenomenon not observed during the control period. This pyloric

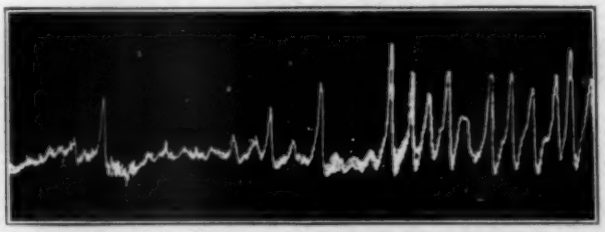

Fig. 12.—Tracing made on Oct. 21, 1935, five months after anterior (left) abdominal vagotomy, showing a persistent decrease in the duration of periods of gastric motility. The duration of this period was twenty-three minutes.

Fig. 13.—Tracing made on Oct. 21, 1935, five months after anterior (left) abdominal vagotomy, showing a persistent increase in the duration of periods of gastric quiescence. The duration of this period was one hundred and eight minutes.

relaxation we feel to be responsible, at least in part, for the decrease in the emptying time of the stomach.

Three observations were made after anterior (left) abdominal vagotomy. The emptying time ranged from two hours and thirty minutes to three hours and fifteen minutes. The average was two hours and fifty minutes, approximately four hours sooner than during the control period. The following is a typical protocol.

May 26, 1935, 7:30 a. m.: The test meal was eaten at this time.

7:45 a. m.: The stomach was estimated to be about four-fifths full. Occasionally deep contractions were observed. A few flecks of barium were seen in the duodenum.

8:00 a. m.: The stomach was estimated to be about half full. Moderate gastric peristalsis was observed. Barium was evident in the small intestine. With each contraction barium was seen passing into the duodenum.

8:30 a. m.: The stomach was estimated to be about one-third full. The remainder of the barium was in the small intestine.

9:00 a. m.: The stomach contained a small amount of barium which was in the pyloric antrum. No barium was seen in the large intestine.

9:30 a. m.: A small amount of barium was still seen in the stomach.

10:00 a. m.: Barium was no longer seen in the stomach. It was distributed throughout the small intestine.

The total emptying time was two hours and thirty minutes.

The following is a protocol of the emptying time of the stomach five months after vagotomy.

Oct. 5, 1935, 8:15 a. m.: The test meal was eaten at this time.

8:20 a. m.: The stomach was estimated to be about two-thirds full. A few flecks of barium were in the duodenum. Weak gastric peristalsis was noted.

8:45 a. m.: The stomach was estimated to be about one-fourth full. A few severe gastric contractions were seen. The barium was distributed throughout the small intestine.

9:45 a. m.: The stomach contained a small amount of barium. The remainder was distributed throughout the small intestine.

10:00 a. m.: The stomach contained a few flecks of barium. The remainder was distributed throughout the small intestine. Barium was not seen definitely in the large intestine.

10:15 a. m.: The stomach was empty. The barium was distributed throughout the small intestine.

The total emptying time was two hours.

COMMENT

Patients with vagotonia may manifest evidence of cardiospasm, gastric hypertonicity, hypermotility, pylorospasm and hyperacidity.[18] These perverted physiologic activities can be verified by the gastrographic, roentgenographic and chemical methods. In our patient there was no evidence of cardiospasm, but gastric hypertonicity and hypermotility were common observations. Intense gastric motility was noted frequently throughout an observation period of five hours. Occasionally the contractions were of sufficient magnitude to rupture the balloon and force bromoform from the manometer. The amplitude of the contractions was definitely increased. This hypermotility was also demonstrable under the fluoroscope. Deep contractions were observed passing over a pylorus, which seemed to be in a constant spastic state.

18. Friedenwald, Julius, and Morrison, Samuel: Vagotonia and Sympatheticotonia in Their Relation to Gastro-Intestinal Disturbances, in Nelson Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1929, vol. 5, p. 168. Eppinger and Hess.[3]

A relationship between the intense motility and the epigastric distress seemed evident. This was disclosed by the patient pressing an electric key which by means of a signal magnet produced an informative mark on the kymograph tracing. Conversely, epigastric distress disappeared when the stomach was quiescent.

Occasionally low grade motility occurred associated with fluctuations in gastric tonus. Since there is evidence [19] to indicate that the vagus nerve may be both motor and inhibitory to the stomach, the reason for this variation is apparent. However, in spite of this, one can deduce from the literature and from the results presented here that the vagus nerve is the primary motor nerve to the human stomach.

Although cardiospasm was not observed in this patient, it nevertheless reflects the influence of the vagus nerve on the cardia. Openchowski [20] found that stimulation of the vagus nerve caused either contraction or relaxation and that the response was due to the frequency and the strength of the stimuli. Courtade and Guyon [21] obtained a motor response and May [16c] reported relaxation of the cardia followed by contracture. Occasionally he noted a pure motor response. Similar results were observed by Meltzer and Auer.[22] Klee [23] and Koennecke [24] obtained closure of the cardia. Carlson, Boyd and Pearcy [25] found that although motor and inhibitory effects were possible, the response of the cardia depended on the tonus at the time of the stimulation of the vagus

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19. Langley, J. N.: On the Inhibitory Fibers of the Vagus for the End of the Esophagus and the Stomach, J. Physiol. **23**:407, 1898. May.[16c] Ivy, A. C.: Applied Physiology of the Gastro-Intestinal Innervation, Am. J. Digest. Dis. & Nutrition **1**:845 (Feb.) 1935.

20. Openchowski, T.: Ueber die nervösen Vorrichtungen des Magens: Experimentelle Studien, Zentralbl. f. Physiol. **3**:1, 1889; Zur pathologischen Anatomie der geschwürigen Prozesse im Magendarmtractus, Arch. f. path. Anat. u. Physiol. **117**:347, 1889; Ueber die gesammte Innervation des Magens, Deutsche med. Wchnschr. **15**:717, 1889.

21. Courtade, D., and Guyon, J.: Contribution à l'étude de l'innervation motrice de l'estomac, J. de physiol. et path. gén. **1**:38, 1899.

22. Meltzer, S. J., and Auer, J.: Vagus Reflexes upon the Oesophagus and Cardia, Brit. M. J. **2**:1806, 1906.

23. Klee, P.: Der Einfluss der Vagusreizung auf den Abbau der Verdauungsbewegungen. Röntgenversuche an der Rückenmarkskatze, Arch. f. d. ges. Physiol. **145**:557, 1912; Beiträge zur pathologischen Physiologie der Mageninnervation: II. Pylorusinsufficienz und präpylorischer Gastrospasmus, Deutsches Arch. f. klin. Med. **129**:275, 1920.

24. Koennecke, W.: Experimentelle Innervationsstörungen am Magen und Darm, Ztschr. f. d. ges. exper. Med. **28**:384, 1922.

25. Carlson, A. J.; Boyd, T. E., and Pearcy, J. F.: Studies on the Visceral Sensory Nervous System: XIII. The Innervation of the Cardia and Lower End of the Esophagus in Mammals, Am. J. Physiol. **61**:14, 1922; XIV. The Reflex Control of the Cardia and Lower Esophagus in Mammals, Arch. Int. Med. **30**: 409 (Oct.) 1922.

nerve. However, Caballero [26] maintained that stimulation of the nerve did not influence the cardiac sphincter.

Our observations on the untreated patient with vagotonia revealed hypertonicity and hypermotility of the stomach. Many gastrographic records exhibited a type of motility similar to that obtained after bilateral resection of the splanchnic nerves,[2] that is, when the stomach was under unopposed control of the vagus nerve. Occasionally low tonus with feeble motility was observed. This, however, was the exception rather than the rule.

It would seem that the occasional variability in the gastric motility observed during the control period and subsequent to vagotomy was due to the fact that the vagus nerve is both motor and inhibitory to the stomach. This was demonstrated by Langley [19] and later confirmed by May [16c] Auer [27] showed in rabbits that only a slight degree of reflex inhibition occurred through the vagus nerve and that normal peristalsis was usually established after one or two days. He found that tracings from the pyloric third of the stomach exhibited no appreciable difference from those obtained from normal animals. Carlson, Boyd and Pearcy,[25] McCrea,[13] and McCrea, McSwiney and Stopford [28] demonstrated that the response to stimulation was governed by the degree of gastric tonus present at the time of stimulation.

Van Braam Houckgeest [29] found that stimulation of the cervical vagus nerve caused contraction of the stomach. Klee [23] obtained only motor effects. Augmentation of peristalsis ensued with a moderately strong stimulus and tonic contraction with a strong stimulus. Bechterew and Mislawski [16a] reported inhibition. They associated the response with the strength of the stimulus. Bercovitz and Rogers [30] and Bercovitz [31] obtained preliminary contraction followed by relaxation. Can-

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26. Caballero, R.: Étude expérimentale de la fermeture de l'extrémité inférieure de l'oesophage (épicardia et cardia), Compt. rend. Soc. de biol. **87**:1359, 1922; Étude expérimentale de la fermeture de l'extrémité inférieure de l'oesophage, ibid. **88**:12, 1923.

27. Auer, J.: The Effect of Severing the Vagi or Splanchnics or Both upon Gastric Motility of Rabbits, Am. J. Physiol. **25**:334, 1910.

28. McCrea, E. D.; McSwiney, B. A., and Stopford, J. S. B.: The Effect on the Stomach of Stimulation of the Peripheral End of the Vagus, Quart. J. Exper. Physiol. **15**:201, 1925.

29. Van Braam Houckgeest, G.: Arch. f. d. ges. Physiol. **8**:163, 1874; cited by McSwiney.[49]

30. Bercovitz, Z., and Rogers, F. T.: The Influence of the Vagi on Gastric Tonus and Motility in the Turtle, Am. J. Physiol. **55**:323, 1920. Rogers, F. T., and Bercovitz, Z.: The Rôle of the Intrinsic Plexuses in Determining the Effect on Gastric Motility of Vagus Stimulation, ibid. **56**:275, 1921.

31. Bercovitz, Z.: The Effect of Vagus Stimulation on Dog's Stomach, Proc. Soc. Exper. Biol. & Med. **19**:228, 1922.

non and Lieb [32] also found that stimulation of the vagus nerve may inhibit the stomach. Daniélopolu [33] observed that compression of the vagus nerve in the neck of man caused inhibition followed by augmented movements. Laughton [34] demonstrated in cats that stimulation of the dorsal vagus nucleus usually caused contractions, but inhibition also occurred if the tonus was high. According to Veach,[35] stimulation with a current of relatively low intensity caused a motor response of the stomach of a cat, while stimulation with a current of high frequency produced inhibition. McSwiney and Wadge [36] could not confirm this. They found that in a condition of low tonus stimulation of the vagus nerve with a current of low or high frequency caused contractions and increased the tonus. In a condition of high tonus, stimulation caused inhibition and relaxation.

The pylorospasm which seemed to be present during the untreated vagotonic state can also be explained on the basis of hyperirritability of the vagus nerve. Crisler and his associates,[37] who observed pylorospasm associated with anoxemia, assumed that this phenomenon was on a "vagospasm basis," since the pylorospasm disappeared when the vagus fibers to the pylorus were cut without disturbing those to the stomach.

Whether changes of tonus in the pylorus are associated with comparable changes in the body and in the fundus of the stomach is still unsettled. Alvarez [38] found that a gradient of muscular rhythmicity may exist which is most marked proximally and which decreases distally

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32. Cannon, W. B., and Lieb, C. W.: The Receptive Relaxation of the Stomach, Am. J. Physiol. **29**:267, 1911.

33. Daniélopolu, D.: Action de l'excitation mécanique du vague au cou sur la motilité de l'estomac chez l'homme, Arch. internat. de physiol. **23**:205, 1924. Daniélopolu, D.; Simici, D., and Dimitriu, C.: Recherches sur la motilité de l'estomac. Action du vague sur la motilité de l'estomac chez l'homme, Compt. rend. Soc. de biol. **91**:493, 1924.

34. Laughton, N. B.: The Effect on the Stomach of Stimulation of the Dorsal Vagus Nuclei, Am. J. Physiol. **89**:18, 1929.

35. Veach, H. O.: Studies on the Innervation of Smooth Muscle: I. The Vagus Effects on the Lower End of the Esophagus, Cardia and Stomach of the Cat, and the Stomach and Lung of the Turtle in Relation to Wedensky Inhibition, Am. J. Physiol. **71**:229, 1925.

36. McSwiney, B. A., and Wadge, W. J.: Effects of Variations in Intensity and Frequency on the Contractions of the Stomach Obtained by Stimulation of the Vagus Nerve, J. Physiol. **65**:350, 1928.

37. Van Liere, E. J.; Crisler, G., and Wiles, I. A.: The Effect of Anoxemia on the Pyloric Sphincter, Am. J. Physiol. **111**:330 (March) 1935. Crisler, George; Van Liere, E. J., and Wiles, I. A.: The Mechanism of the Delay in Gastric Emptying Time Caused by Anoxemia, Am. J. Digest. Dis. & Nutrition **2**:221, 1935.

38. Alvarez, W. C.: The Mechanics of the Digestive Tract, New York, Paul B. Hoeber, Inc., 1922.

toward the pylorus. However, Brown and McSwiney,[39] working on isolated muscular strips, were unable to confirm this. McCrea's observations [18] showed that the vagus nerves regulate both tonus and movements and that these may be independent of one another. Courtade and Guyon [21] and Carlson, Boyd and Pearcy [25] also noted that the effects obtained on stimulation depend on the existing condition or tonus.

The results reported in the literature regarding the effect of stimulation of the vagus nerve on the pyloric sphincter are conflicting. Langley [19] demonstrated that the body of the stomach and the pylorus received inhibitory as well as motor fibers from the vagus nerve. This was confirmed by May.[16c] Carlson and Litt [40] reported contracture of the pylorus when there was low or moderate tonus and occasionally relaxation in the hypertonic or spastic stomach. Van Izeren [41] obtained contracture. One of us [42] observed pylorospasm after stimulation of the peripheral stump of the cut cervical vagus nerve. The evidence indicated that the vagus and splanchnic nerves carry both motor and inhibitory impulses to the stomach as a whole as well as to the pyloric sphincter and that the subsequent result of stimulation is governed by the tonus or peripheral mechanism at the time of the stimulation.

Thomas and Wheelon [43] found that stimulation of the vagus nerve produced an increase in the tonus and an increase in the force and frequency of the rhythmic contraction of the pyloric sphincter. They finally concluded that the pyloric sphincter received a double nerve supply consisting of motor and inhibitory nerves by way of the vagus and splanchnic nerves; these nerves, however, are mainly motor in function. Inhibitory fibers may be found in these nerves but more are found in the splanchnic nerves than in the vagus nerve.

Atropine in large doses produced considerable symptomatic relief in this patient. Associated with the clinical improvement, the kymographic records revealed a decrease in the duration of the period of gastric motility with a slight increase in the period of gastric quiescence. The number and amplitude of the contractions were slightly decreased. There was a slight increase in the interval between contractions. An analysis of the results obtained by other investigators revealed that these findings have a sound physiologic basis.

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39. Brown, G. L., and McSwiney, B. A.: The Movements and Reaction to Drugs of Strips of the Gastric Musculature of the Cat and Dog, Quart. J. Exper. Physiol. **16**:9, 1926.

40. Carlson, A. J., and Litt, S.: Studies on the Visceral Nervous System: On the Reflex Control of the Pylorus, Arch. Int. Med. **33**:281 (March) 1924.

41. Van Izeren: Ztschr. f. klin. Med. **43**:181, 1901; cited by McSwiney.[40]

42. Barron, Louis E.: Unpublished studies.

43. Thomas, T. E., and Wheelon, H.: The Nervous Control of the Pyloric Sphincter, J. Lab. & Clin. Med. **7**:375, 1922.

Smith,[44] working on the surviving strips of the stomach of various animals, demonstrated that pilocarpine caused contractions of all parts of the stomach which were inhibited by atropine. Tezner and Turolt [45] confirmed the inhibitory effect of atropine on the human stomach. Brown and McSwiney,[39] working on muscle strips, found that pilocarpine stimulated the motor action of the vagus nerve. Atropine produced inhibition. It is the opinion of Carlson, Boyd and Pearcy,[25] Batelli [16b] and McCrea and MacDonald [46] that atropine paralyzes the gastric musculature, eliminating control by both the vagus and the splanchnic nerves.

There is sufficient evidence to show [13] that bilateral vagotomy should not be done in the neck, since esophageal and laryngeal paralysis ensue with subsequent death from infection of the respiratory tract. Intrathoracic or abdominal vagotomy can be accomplished with a relative degree of safety.

Certain investigators [47] have reported that either the right or the left vagus nerve may innervate the entire stomach. Bechterew and Mislawski,[16a] Batelli [16b] and May [16c] have noted that stimulation of the left vagus nerve may cause a greater effect than stimulation of the right. Laughton [34] also found that faradic stimulation of the cephalic half of the left dorsal vagus nucleus resulted in a more marked effect on the stomach than stimulation of the corresponding part of the right dorsal vagus nucleus. McCrea and his associates [48] and McSwiney [49] reported that unilateral vagotomy was without effect.

Our results were striking after anterior (left) abdominal vagotomy. We observed a definite decrease in the duration of the period of gastric motility associated with an increase in the duration of the period of gastric quiescence. One of the outstanding results was the marked increase in the interval between contractions. In one instance it was as much as twelve minutes. The number and amplitude of the contractions were decreased. The resulting hypotonus was striking.

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44. Smith, M. I.: The Action of the Autonomic Drugs on the Surviving Stomach, Am. J. Physiol. **46**:232, 1918.

45. Tezner, O., and Turolt, M.: Studien über die Wirkung der Verschiebung der K- und Ca- Ionen auf den überlebenden menschlichen Magen, Ztschr. f. d. ges. exper. Med. **24**:1, 1921.

46. McCrea, E. D., and MacDonald, A. E.: The Action of Drugs upon the Movements of the Stomach, Quart. J. Exper. Physiol. **19**:161, 1928.

47. Ducceschi, U.: Sui nervi dello stomaco, contributo alla conoscenza della innervazione viscerale, Arch. di fisiol. **2**:521, 1905. Morat, J. P.: Sur quelques particularités de l'innervation motrice de l'estomac et de l'intestin, Arch. de physiol. **5**:142, 1893. McCrea.[15a]

48. McCrea.[13] McCrea, McSwiney and Stopford.[17]

49. McSwiney, B. A.: Innervation of the Stomach, Physiol. Rev. **11**:478, 1931.

Carlson [50] maintained that section of the vagus nerve left the stomach on the whole hypotonic for at least three months. Observations on our patient five months after vagotomy revealed persistent hypotonus at this time. However, Cannon [51] reported that section of the vagus nerve resulted in only temporary loss of gastric tonus and a slowing or weakening of the peristalsis. It would appear that this loss of tone is the result of the subsequent inhibitory action of the splanchnic nerves. We concur with the findings of McCrea and his associates [52] that experimentation immediately after vagotomy yields unreliable results because of anesthesia and shock. We feel that it is necessary to permit at least a week for convalescence before the effect of vagotomy can be accurately evaluated.

An abnormal retention of gastric contents was observed in our patient during the untreated vagotonic state. With a test meal consisting of 3 ounces of Cream of Wheat, 2 ounces of barium sulfate and sufficient water to form a paste, the total preoperative emptying time in one instance was as much as eight hours. The average emptying time during the control period was six hours and forty-nine minutes. A test meal of moderately thick consistency was intentionally selected in order to avoid some of the discrepancies reported by Meek and Herrin.[53] It would seem at this time that the probable cause for this abnormal gastric retention was the pylorospasm obstructing the outlet of the stomach.

Under the influence of large doses of atropine, there was a slight decrease in the emptying time of the stomach. The average time was five hours and twelve minutes, making an average difference of one hour and thirty-seven minutes. The pylorus appeared to be less spastic under this medication. Associated with this there was mild symptomatic improvement.

Striking results followed left abdominal vagotomy. The average total emptying time was reduced to two hours and fifty minutes, an average difference of approximately four hours. During this period particles of barium could be seen passing through a relaxed pylorus, an observation which was not noted during the control period. Our results concur with those of McCrea and MacDonald [46] in that this reduction in the emptying time is probably the result of a patulous pylorus. Observations made five months after vagotomy revealed an

50. Carlson, A. J.: Hunger in Health and Disease, Chicago, University of Chicago Press, 1916.

51. Cannon, W. B.: Mechanical Factors of Digestion, New York, Longmans, Green & Co., 1911.

52. McCrea.[18] McCrea, McSwiney and Stopford.[17] McCrea and MacDonald.[46]

53. Meek, W. J., and Herrin, R. C.: The Effect of Vagotomy on the Emptying Time, Am. J. Physiol. **109**:221, 1934.

emptying time of two hours, a difference of four hours and forty-nine minutes. Associated with this marked decrease in the total emptying time, there was definite symptomatic improvement.

Meek and Herrin [53] emphasized the fact that the consistency of the test meal was responsible for certain discrepancies reported in the literature. They stated that the evidence pointed to the vagus nerve as being necessary for the existence of gastric tonus and that the emptying depended on the degree of this tonus. They finally concluded that gastric tonus depended on the innervation of the vagus nerve and that vagotomized animals have almost entirely lost gastric tonus. They assumed that the initial decreased emptying time was due to the loss of tonus and the subsequent gravitation of fluids through the pylorus.

McCrea, McSwiney and Stopford [17] observed that after unilateral vagotomy there were paresis and dilatation of the stomach with delay of all motor functions, which they attributed to shock. This persisted for about six days. Paresis then disappeared, and normal function was restored. Observations were made up to twenty-two months, but no change was noticed in the condition of the stomach. After bilateral vagotomy there was a marked decrease in the initial emptying time as well as some decrease in the total emptying time. The early initial emptying of the stomach was the most prominent permanent feature of vagotomy. The authors attributed this to a semipatulous condition of the pyloric sphincter. A decrease in the total emptying time was observed in about 50 per cent of their animals.

Hughson [54] did not observe acute dilatation of the stomach after section of the vagus nerve. He concluded that section of this nerve in dogs, either at the cardia or on the anterior and posterior walls of the stomach, caused a decrease in the normal emptying time of the stomach.

Opposite results were obtained by Latarjet and Wertheimer.[55] They found that total resection of the branches of the vagus nerve produced dilatation and atony of the stomach and that these effects were permanent. The contractions seen by them roentgenographically were weak and widely spaced. They noticed a marked delay in the emptying time of the stomach and reported that section of any branch of the vagus nerve resulted in atony of the wall of the stomach with vasodilatation of the vessels in the portion supplied by the sectioned branch. Stimula-

54. Hughson, Walter: The Effect of Vagus Neurotomy on the Pyloric Sphincter, J. A. M. A. **88**:1072 (April 2) 1927; Reflex Spasm of the Pylorus and Its Relation to Diseases of the Digestive Organs, Arch. Surg. **11**:136 (July) 1925.

55. Latarjet, Cluzet and Wertheimer: Effets de la section et de l'excitation des nerfs propres de l'estomac sur la motricité de cet organe, Compt. rend. Soc. de biol. **84**:985, 1921.

tion of any of the branches produced hypermotility in the part supplied by the branch. After total section, they observed a relaxed pylorus.

Many deleterious effects have been reported after vagotomy. Our studies have not substantiated any of these reports. Alvarez,[56] from his work on rabbits, reported a mortality of 49 per cent after vagotomy. In many animals death was due to diarrhea and inanition. Auer [27] reported the occurrence of ulcer in a number of his vagotomized rabbits. However, this relationship is rarely observed in the stomach of man or of the cat or dog. Donati [57] obtained negative results in dogs. Greggio [58] found ulcers in only a small percentage of his dogs. Durante [59] reported that lesions of the gastroduodenal nerves, that is, the vagus and the sympathetic nerves, may produce ulcers. Koennecke [24] observed hemorrhagic and thrombotic processes throughout the gastro-intestinal tract in a dog subsequent to bilateral subdiaphragmatic vagotomy. Ivy [60] found that dogs dying immediately after section of the vagus and the splanchnic nerves not infrequently show petechial hemorrhages of the pyloric and duodenal mucosa. However, there were several dogs with no gastric or duodenal lesions after resection of the vagus and splanchnic nerves. Most of Ivy's animals lived indefinitely, and section of the nerve was verified at necropsy. Repeated clinical and roentgenographic examinations of our patient failed to reveal any evidence of gastro-duodenal ulcers throughout any period of the investigation. There was marked subsequent clinical improvement with the complete disappearance of gastro-intestinal distress after vagotomy.

CONCLUSIONS

Hypermotility and hypertonicity of the stomach were observed in a patient manifesting the symptom complex of vagotonia as described by Eppinger and Hess.[3] Associated with these findings there appeared to be pylorospasm. The hypermotility and hypertonicity were associated gastrographically and fluoroscopically with epigastric distress.

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56. Alvarez, W. C.: The Effect of Degenerative Section of the Vagus and Splanchnic Nerves on the Digestive Tract, Proc. Staff Meet., Mayo Clin. **4**: 205, 1929; The Effect of Degenerative Section of the Vagus and Splanchnic Nerves on the Digestive Tract, Am. J. Physiol. **90**:631, 1929.

57. Donati, M.: Experimentelle Versuche das Magengeschwür vermittels Verletzungen der Magennerven hervorzurufen, Zentralbl. f. Chir. **31**:346, 1904; Arch. f. klin. Chir. **73**:908, 1904.

58. Greggio, E.: Des ulcères gastro-duodénaux, Arch. de méd. exper. et d'anat. path. **28**:533, 1917.

59. Durante, L.: The Trophic Element in the Origin of Gastric Ulcer, Surg., Gynec. & Obst. **22**:399, 1916.

60. Ivy, A. C.: Contributions to the Physiology of the Stomach: LII. Studies on Gastric Ulcer, Arch. Int. Med. **25**:6 (Jan.) 1920.

During intense medication with atropine there was a slight decrease in the duration of periods of motility. This was associated with a slight increase in the duration of the periods of quiescence. A slight decrease in the number and amplitude of the contractions associated with a slight increase in the interval between contractions was also noted. This slight decrease in gastric tonus was associated with mild symptomatic relief.

After anterior (left) abdominal vagotomy there ensued a marked decrease in the duration of periods of motility associated with a marked increase in the duration of periods of gastric quiescence. The number and amplitude of the contractions were noticeably diminished. The interval between contractions was markedly increased.

An analysis of studies of the gastric motility made five months after vagotomy revealed that the decrease in the duration of periods of motility and the decrease in the tonicity of the stomach were still evident.

During the untreated stage the emptying time of the stomach was delayed. This we would attribute to pylorospasm.

During medication with atropine the stomach emptied its contents one hour and thirty-seven minutes sooner than during the control period.

After left abdominal vagotomy the stomach evacuated its contents four hours sooner than during the control period.

Five months after vagotomy this decrease in the emptying time still persisted.

There was no evidence at any time of acute dilatation of the stomach.

The results of vagotomy were attended by definite symptomatic improvement. At no time could we obtain clinical or roentgenographic evidence of subsequent lesions of the gastro-intestinal tract.

Mrs. Jean Barron rendered valuable assistance in the interpretation of the kymographic tracings.

SCOLIOSIS

A FUNCTIONAL DECOMPENSATION

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Scoliosis may be defined as an abnormal, persistent lateral curvature of the spine with symptoms due to functional decompensation of the back.

The history of scoliosis dates back to the most ancient known civilization. The presence of the lateral curvature of the spine was familar to the ancient Egyptians. Hippocrates left a description of scoliosis and even suggested a remedy. However, the actual understanding of scoliosis has remained obscure. One of the important steps in the development of present day knowledge occurred at the time of Hessing. Hessing was a mechanical genius who made a form-fitting brace which gave sufficient support to the back so that a patient with scoliosis who wore one of these braces received definite benefit. This was the beginning of the supportive treatment for scoliosis. The opposing school developed under Ling in Stockholm. Ling had the conception of making a perfect body by developmental exercises. The use of the various types of exercises and corrective strengthening received its great impulse from the fact that marked improvement was noted as a result of gymnastic therapy. Later, orthopedic surgeons developed the combination of supportive and corrective treatment. In addition, they have added much to the understanding of the condition both as to its development and as to its etiology.

Before going on to a discussion of the pathologic process of scoliosis, it is essential to define some of the common terms used in describing the condition. The terms primary curve and secondary curve are frequently used; the primary curve is the original curve, and the secondary curve is the compensatory curve. Anatomically, one speaks of a right or left curve, depending on the direction of the deviation. The term "structural scoliosis" is sometimes used to describe the presence of abnormalities in the bones and ligaments. If the curve is a single simple curve, it is spoken of as a C curve; if there is a compensatory curve present, it is called an S curve. Usually the lateral curvature is associated with torsion of the vertebral column; this is termed rotation. The location in which the curvature occurs is used further to define the scoliosis; for instance, one speaks of right lumbar or left lumbar scoliosis. The changes in the bone and in the soft tissues tend to limit the motion of the spine and to bring about what is clinically known as fixation; it limits one of the functions of the back, that of motion, but aids the more important function of maintaining the erect posture of the body. When

the back is capable of carrying out this function, it is said to be sufficient; an insufficiency arises when there is weakness in the structures of the back or when the normal back is overstrained by too great a load.

MORBID ANATOMY

The structural changes that occur make up the actual morbid anatomy. The primary structural changes are those which give rise to scoliosis; the secondary structural changes result from the altered statics brought about by the curvature. The bony changes that occur as primary structural changes are congenital malformations of the vertebrae and the destruction of the vertebrae by disease such as tuberculosis, osteomyelitis or tumor. Secondary bony structural changes consist in the altered shapes of the vertebrae. The vertebrae are wedge shaped, with the narrow margin toward the concavity. The articular facets are broader and more horizontally placed than normal. The intervertebral foramina are narrowed; the transverse process on the concave side is narrower than normal, and the vertebral foramen is egg shaped instead of round. The presence of strain and irritation frequently causes overgrowth or exostoses at the vertebral margins; at times these are extensive enough to cause a certain degree of fixation. With the presence of strain there is loss of joint space, particularly at the convex side, between the vertebrae. The intervertebral disks are compressed and become wedge shaped. A certain amount of fibrous change occurs in the disks; the joint surfaces become irregular, and there is loss of cartilage until actual fusion occurs. The ligaments accommodate themselves to the altered position of the spine and are stretched on the convex side and short and thick on the concave side of the curvature.

The changes in the muscles vary with the different types of scoliosis, as, for instance, the muscular changes seen in scoliosis caused by spastic hemiplegia and those associated with scoliosis caused by infantile paralysis. In the latter there is an actual flaccid paralysis which may involve any one group or even individual muscles of the back or abdomen, while in the former there are hypertonic muscles on one side. In the adolescent type of scoliosis the muscles on the convex side are thin and stretched and show fibrous changes while the muscles on the concave side are shortened and may show fatty degeneration. Other anatomic changes that occur concomitant with the lateral curvature are an increased posterior curve in the dorsal area (rounded kyphosis) and an increased anterior curve in the lumbar region (lordosis). Rotation is frequently present, and the effect on the chest is marked. The ribs, which act as long levers attached to the vertebral column, show a marked deformity; the result is compression of the wall of the chest on one side. Frequently this distortion is so marked as to interfere with the normal use of the lung, and at times it compresses the heart or even the aorta and vena cava.

In order to understand the development of the curvature which makes up the scoliosis, a few normal anatomic and physiologic facts should be emphasized. Significant is the fact that there are normally present four anteroposterior curves.[1] The primary curves are a posterior curve in the dorsal area and a posterior curve in the sacral area. The anterior curves in the lumbar and cervical areas develop after the child assumes an upright position, and these are therefore considered compensatory or secondary curves. One lateral curve is normally present in the dorsal area; this is usually to the right, although it may be to the left, the variations being dependent on race, occupation and other factors.

Of physiologic importance is the fact that the primary function of the back is to hold the upright position;[2] furthermore, the human body will always attempt to assume the upright position. Movement in the dorsal area is relatively limited, 80 per cent of the motion of the spine being in the lumbar area. In addition, one must remember that structures will grow, within limits, according to the demand made on them. It is not difficult to understand the development of a lateral curvature secondary to a tilt in the pelvis; the lateral curvature is compensatory in order for the body to retain the upright position. Similarly, there is a compensatory dorsal lateral curvature in the presence of torticollis. Relatively easy to understand, also, is the lateral curvature of the spine caused by the contracture of the pleural cavity. That spastic paralysis of one side would cause some degree of lateral curvature is to be expected. The imbalance in weight bearing caused by a laterally wedge-shaped vertebra, whether due to a congenital anomaly or to destruction by disease, gives rise to scoliosis. The explanation of the curvature in anterior poliomyelitis is more involved. It is readily seen that a curvature will develop when the muscles on only one side of the back are paralyzed; however, there are scoliotic curves which develop when paralysis in the muscles is relatively symmetrical. The development of the curves in these cases may be explained on the same basis as those in the so-called adolescent type of scoliosis.

Rachitic scoliosis is due to a softening of the structures, particularly the bony structures in the vertebrae; hence, when normal stress is applied there is a tendency for an increase of the normal lateral curvature with the development of compensatory curves. The severity of the curvature is dependent on the degree of weakness caused by the rickets as well as on the amount of stress applied.

Adolescent scoliosis is so called from the period at which it most frequently occurs, but like rachitic scoliosis, it is due to a weakness in

1. Morris, H.: Human Anatomy, edited by C. M. Jackson, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1933, p. 103.

2. Magnus, Rudolf: Some Results of the Studies in the Physiology of Posture, Lancet **2**:531-536 (Sept. 11); 585-588 (Sept. 18) 1926.

structure. The primary weakness is in the muscles,[3] although the ligaments and bones show some loss of strength. If there is an imbalance between the capacity of the back to do its normal work and the demand made on the back there will ultimately be an increase in all the normal curves; therefore, the first physical sign is usually an increase of the anteroposterior curves, which is recognized as poor posture. If the imbalance continues, the lateral curvature will also increase and scoliosis will develop; ultimately there will be compensatory curves to the dorsal curve in the lumbar and cervical areas. Therefore, scoliosis develops whenever there is a decrease in strength of the structures of the back (loss of capacity) or if there is an increase in the demand made on the back (overload), or a combination of the two. In the presence of such a condition, decompensation develops; the word insufficiency is sometimes used for decompensation. The decompensation refers to an imbalance in the function and gives rise to symptoms of fatigue and strain. A prolonged period of decompensation will result in an increase in all the normal curves, which means a lateral curvature; this condition is called scoliosis. With the occurrence of lateral and anteroposterior curvatures, the effect on the vertebral column must be torsion or rotation. The greater the decompensation and the more prolonged the duration of the scoliosis, the more severe the curvature will be and the more marked the actual structural changes.

ETIOLOGY

The various clinical forms of scoliosis are best classified on the basis of etiology. There are, first of all, two distinct types—congenital and acquired.

The congenital scolioses are of one of two types. 1. The first type is due to an anomaly. There is a definite deformity which can be demonstrated roentgenographically; the lateral side of one or of several vertebrae is only partially formed, or one or more vertebrae may be absent, resulting in a relatively sharp lateral curvature in the direction opposite the involved side. In cases of severe involvement there will be a compensatory curve above and below this primary curvature. In many instances, however, the structure, even though badly formed, will be highly efficient, and there will be no decompensation. In such cases the deformity is the only abnormality, and the prognosis for any change in the deformity is practically nil; on the other hand, no symptoms in the way of impaired function will develop. 2. The second type of congenital scoliosis is probably due to the prolonged retention of the lateral posture in utero; in this type there is the simple C curve. The roentgenographic picture is normal; the curvature, however, tends to persist, particularly when the body assumes the upright position; the spine is

3. Hauser, Emil: The Muscle Factor in Adolescent Scoliosis, J. A. M. A. **98**:1535-1538 (April 30) 1932.

pliable. With corrective measures the prognosis for full recovery, both anatomically and functionally, is excellent.

Aquired scolioses may be divided as into the following types.

Curvature Due to Rickets of Osteomalacia.—The existence of fetal rickets and its relationship to scoliosis is still problematic. The occurrence of static deformities and the presence of rickets are well known. Owing to softness and weakness in the structures of the back, there is an increase of all the normal curves; so there may be rachitic kyphosis as well as the rachitic scoliosis. The roentgenogram shows changes in the bone. The presence of the other signs of rickets helps to establish the diagnosis. Usually rachitic scoliosis is severe. The prognosis is dependent on the early recognition of the condition. If a highly developed curve has been allowed to persist until the child has reached adolescence, little can be done in the way of correction of the deformity. The prognosis as to function, however, is relatively good.

Scoliosis due to osteomalacia may be explained in the same manner. The condition, fortunately, is rare; the prognosis is poor.

Scoliosis Due to Flaccid Paralysis (Anterior Poliomyelitis).—Scoliosis due to infantile paralysis presents the most bizarre forms. This is to be expected in view of the various muscles affected, as well as the varying degrees of paralysis present in each muscle. A marked asymmetrical paralysis will definitely affect the degree of the curvature. The most severe types of scoliosis seen occur as the result of infantile paralysis; one sees not only the highest degree of deformity but, owing to the paralysis, marked incapacity. In connection with poliomyelitis, it has been observed that paralysis of the abdominal muscles will give rise to a scoliotic curvature. The explanation offered is that it is impossible for the muscles of the back to act as the function of the abdominal muscles, which act as opponents, is completely lost. The inability of the muscles to act results in a loss of normal function of the back, namely, to hold the erect position; the result is an increase of the curvatures, including the lateral curvature, and, therefore, scoliosis. The prognosis in these cases is dependent on the amount of recovery possible in the nerves and, ultimately, in the muscles. The early paralysis, owing to edema, will, if properly cared for, permit recovery in strength. The prognosis, therefore, depends on adequate treatment in the early stages and on the development of power in the remaining muscles. If the paralysis is so severe that even with proper treatment there is insufficient strength to hold the upright position, scoliosis will inevitably result. The severity of the scoliosis and the amount of disability can be controlled, to some extent, by supportive measures. In this connection it is important to realize that there is a natural tendency in the body to create a fixation which will increase the stability as well as the capacity of the back. The curvature ultimately reaches a point where it becomes fixed and acquires a certain degree of compensation so far as function is con-

cerned, so that with limited functional demands the patient may be relatively free from symptoms in spite of a deformity. Of course, with the severe deformities there are decrease of vital capacity and impairment of cardiac function, which means a shortening of life expectancy.

Scoliosis Associated with Syringomyelia.—It is estimated that 80 per cent of all persons with syringomyelia have an associated scoliosis; in fact, it is one of the first symptoms to appear. The curvature is usually higher than in other types of scoliosis; characteristic also is the fact that it is slow in acquiring fixation; in other words, it remains mobile for a long time. The severity of the condition varies. In late stages kyphosis and deformity of the chest develop. The cause of the scoliosis is not certain. It is believed that it is due to trophic disturbances in the bone. The pathologic process is a spastic paralysis with dissociation of sensation—retention of touch and loss of heat and pain senses. Among the trophic changes are swelling in the hands, thickening of the skin and arthropathies. The lesion is in the spinal canal and may be a gliosis, a tubelike cavity or a degenerative change in other parts of the cord due to pressure. The primary condition is usually progressive, which, of course, determines the prognosis.

Curvature Due to Spastic Palsy (Hemiplegia).—When spastic paralysis involves one side of the body, a lateral curvature develops in an effort to establish a balance; this is, to a certain extent, a compensatory curvature. The prognosis is dependent on the possibility of clearing up the spastic paralysis. This type of scoliosis does not give rise to a functional disturbance.

Scoliosis Secondary to Deformities Elsewhere in the Body (Static Deformity).—Any deformity that causes a pelvic tilt, such as an anomaly in the development of the pelvis or shortening of one limb as a result of anterior poliomyelitis, tuberculosis, fracture, epiphysial slipping, contractures of the hip and knee, dislocations of the hip or unilateral genu valgum, will give rise to a lateral curvature in the lumbar area; compensatory curves may develop, giving rise to an S-shaped scoliosis. The curve develops in compensation for the malposition of the pelvis and is the result of correction, to enable the body to hold the erect position. The prognosis is dependent on the possibility of correcting the pelvic tilt. The condition usually is not progressive.

Scoliosis Due to Torticollis.—The presence of torticollis, whether congenital or acquired, gives rise to a secondary compensatory curve in the dorsal area. A one-sided cervical rib would have the same effect. This type of scoliosis may also develop secondary to a congenital elevation of the shoulder. The prognosis in these cases is dependent on the possibility of correcting the primary deformity.

Curvature Due to Local Disease of the Spine.—Any lesion that destroys the lateral part of one or of several vertebrae will result in an

angular type of scoliosis in that area; secondary curvatures will develop later. Tuberculosis occasionally causes such a destruction. At times one sees the same type of scoliosis as a result of a malignant condition. Rarely, a fracture of the vertebral body will give rise to a lateral curvature. The scoliosis in such cases is of relatively minor importance in comparison with the primary disease.

Curvature Secondary to Contracture of the Chest.—A contracture in the wall of the chest, whether due to pleurisy or thoracoplasty, will result in a lateral curvature in the dorsal area. Rotation occurs early in this type of scoliosis. The ribs exert an influence on the spine so as to cause rotation and lateral curvature. The prognosis is good so far as the arrest of the progress of the deformity is concerned.

Lateral Curvature Due to Sacro-Iliac Disease or Sciatica.—In reality such a curvature is a protective list and not true scoliosis. The curvature or list will subside if the pain is relieved.

Hysterical Scoliosis.—This type of scoliosis occasionally occurs in women and, in rare instances, was seen in men during the World War. Usually other signs of nervous irritability are present. Of diagnostic value is the fact that the scoliosis disappears under anesthesia.

Adolescent Scoliosis.—This type of scoliosis has also been called idiopathic, static, occupational, habitual, postural or simple scoliosis. The term "idiopathic" should be eliminated as obsolete, as the etiology no longer remains unknown. The scoliosis develops secondary to a functional insufficiency of the back. Anything that decreases the normal capacity of the back or increases the load beyond normal, or a combination of these factors, will tend to give rise to an adolescent scoliosis. One of the principal factors that decrease the normal strength of the back is the rapid growth that occurs during the period of adolescence. Debilitating diseases lower the strength of the back, which accounts for the scoliosis which occurs after scarlet fever. In children physically below par, if they are not guarded, scoliosis slowly develops. This failure of sufficient structural development may be due to the lack of proper food. Insufficient air and sunshine will act as additional factors; inadequate physical exercise is an important factor. The introverted child with studious tendencies and poor muscular coordination is prone to lateral curvatures of the spine. The load may be increased unilaterally by the carrying of heavy books on one arm. Most important, however, is the abuse of the primary function of the back, namely, the holding of the erect position of the body. If this function is unduly prolonged, a strain will result. Formerly this was a frequent occurrence among school children. At times the load may be increased by excessive body weight. Usually it is a combination of several of these factors over a relatively prolonged period of time that accounts for the development of scoliosis during adolescence. It is possible that rickets may also play a rôle,

particularly the so-called "late rickets." Unrecognized congenital malformations, particularly in the fifth vertebra, may play a more important part than is realized in the development of scoliosis during adolescence. In this country adolescent scoliosis occurs more frequently than all the other types combined. This is not true in European countries where scoliosis due to rickets occurs more frequently than the other types. It is difficult to say just when the adolescent scoliosis develops. Children usually are brought in for attention during the school age; the average age seems to be about 13 years. It is evident that the curvature arises some time previous to the time of examination.

With regard to symptoms, in the incipient stage adolescent scoliosis is a simple C curve in the dorsal area. Right dorsal and left lumbar curves occur in about 80 per cent of the cases; in the other 20 per cent the curves are inverted, that is, left dorsal and right lumbar curves. Rotation appears by the time the posterior curves develop. In the dorsal area the ribs emphasize the rotation, and the deformity of the chest is marked, while in the lumbar region the transverse processes are comparatively short, and the rotation, although equally great, is not apparent. In the usual form of scoliosis the left shoulder drops lower than the right; the right scapula projects posteriorly and is high; the left wall of the chest is compressed posteriorly, with the ribs curved downward. The vital capacity is diminished; the shoulders droop forward, and the normal lumbar curve is accentuated. The torso seems to be shortened, and the body tends to list toward the affected side. The patient usually complains of fatigue and backache. These are the chief symptoms of muscular insufficiency of the back. In cases of extreme involvement the nerve is impinged, causing severe pain along its distribution. There is inability to carry out normal exercises. Frequently there is an associated awkwardness; many of the children are extremely sensitive and shy and have an inferiority complex.

The curvature usually grows progressively worse if left untreated, provided the causative factors continue to exist. In many instances the causative factors are removed without actual recognition of their importance. Complete recovery may result. Even when a curvature has developed, the condition in some cases is arrested simply by means of participation in athletic sports; on the other hand, strenuous athletics may increase the deformity.

The principal complications have already been indicated under symptoms—cardiac decompensation, decrease of vital capacity and altered psychology.

The prognosis in cases in which treatment has been given is variable, depending on the extent and severity of the scoliosis. In extreme scoliosis of long standing it is impossible to obtain complete correction of the deformity; in the early stages satisfactory correction and retention of normal position can be accomplished. The best prognosis is held

in those cases in which the first signs of the lateral curvature are recognized and prophylactic treatment is immediately instituted. In the cases of severe involvement, even though the deformity cannot be corrected, the functional capacity can be greatly increased.

TREATMENT

The object of treatment in scoliosis is twofold: the reestablishment of normal function and the correction of the deformity.

In reviewing the methods of treatment, only those which offer some definite principle are included. With the introduction of the form-fitting corset by Hessing, supportive treatment was first used to give relief from the strain and to bring about some correction. These corsets were of several types. They were applied with the body extended, with reenforcements beneath the convexity; counterpressure was applied to the sacrum. The principle involved in the Hessing corset is used in modern treatment.

The principle of exercise in various forms has been recommended, for example, passive exercise, in which force is directed against the convexity, and active exercise; the latter has been found the more satisfactory. Various systems have been devised; however, more important than the particular system used is the fact that the exercises are graduated to the needs of the patient. Exercises to increase the strength of the muscles only on the side of the convexity were used for many years. Some even went so far as to attempt to reduce the strength on the concave side. It was found that all exercises that increased the strength of the muscles, whether the muscles of the abdomen, back or shoulder or of the pelvic girdle, were beneficial in the treatment of scoliosis. Greater mobility is possible with the body in the horizontal position, and exercises on the hands and knees were prescribed. By the same token, swimming can be considered a beneficial exercise, particularly as an early exercise for weakened muscles. Corrective exercises in which the patient voluntarily stretched the body by means of a Sayre attachment to the head have been used. Many types of apparatus consisting of mechanical levers to increase the force have been invented. Some of these have been combined with mechanisms for extension.

Correction by means of hyperextension frames and by plaster of paris beds, in which the body was held in a corrected position, has been attempted. The disadvantage of prolonged hospitalization and rest in bed is the resultant increase in structural weakness.

Treatment by means of forceful correction, with retention of the corrected position by means of a plaster of paris cast, has been tried. Abbott developed this type of treatment to a high degree. However, the severity of the pain, the development of pressure sores and the inability to increase the strength during treatment ultimately made it necessary to abandon this form of correction.

Derotation is another fundamental principle in the correction of the scoliotic deformity. This has been attempted by means of elastic straps passing over the shoulder and down around the pelvis and acting as a derotating coil. Another method fixes the chest in a vice; the pelvis is fixed on a seat that can be tilted and rotated; with the upper part of the body fixed, the pelvis can then be turned to bring about a derotation. When the desired position is attained, the chest, the trunk and the pelvis are held with a plaster of paris cast. Correction can be obtained in this manner, but again it is difficult to reestablish the capacity to retain correction. A more simple method to obtain the same result is to fix the pelvis by means of a horizontal bar on an upright frame and to derotate by turning the shoulder girdle, using the arms as levers.

The treatment of scoliosis is dependent on the etiologic factors. In congenital scoliosis the presence of an anomaly does not permit the actual removal of the causative factor. Attempts have been made to remove the hemivertebra in order to balance the spinal column. Surgical removal can actually be carried out, but the improvement obtained does not justify the procedure. Furthermore, it is questionable whether the capacity is not decreased rather than increased. The most important part of treatment is to prevent a further increase of the curvature. This is best accomplished by the use of functional exercise, that is, by treating the child as though it were normal. In other words, the use of braces, unless there is an additional factor, is contraindicated.

Congenital scoliosis due to intra-uterine posture can be corrected even before the child is able to sit up. If the deformity tends to persist, it may be advisable to use a plaster of paris bed with the curvature in the opposite direction. The child can sleep in such a bed, and correction is attained. Furthermore, the parents can hold the child in such a way that there is a tendency for the deformity to be corrected. If the curvature is not recognized until the child begins to walk, it is occasionally necessary to apply a plaster of paris jacket, with the child held in the overcorrected position. Once such a jacket is applied, it is important to make certain that exercises are carried out to keep up the general strength of the body. The more rapidly this correction can be attained and all supportive treatment discontinued, the better the result.

In the treatment of scoliosis due to rickets, the problem is twofold. In active rickets the process of deformity is progressive. During this period correction can be attained; this can be done by means of casts and braces. However, of primary importance is the treatment of the rickets itself; this, of course, includes a complete antirachitic regimen. The earlier this is instituted the more satisfactory the result. The scoliotic deformity may progress after the actual rickets has subsided; this deformity is fixed. Only in the preadolescent stage is there hope for improvement so far as correction of the curvature is concerned. Of prime significance, therefore, is the attainment of the maximum amount

of function. When this is accomplished, even though the deformity may persist, the child will be able to lead a normal, useful life.

Scoliosis due to anterior poliomyelitis offers the most difficult phase of the scoliotic problem. The final solution of the problem must be the prevention of infantile paralysis. The early recognition of the involvement of muscles of the abdomen and back in cases of poliomyelitis and the protection of such muscles until they regain the maximum amount of strength are of primary importance. In the reestablishment of strength, exercises are essential; under-water therapy and swimming are important. The back must be protected against the development of a curvature. In this connection, the patient should be permitted to sit or stand for only a brief period; as the strength of the muscles increases, the length of time may be gradually increased. The use of massage and muscle training is essential, as in any case of paralysis. In those cases in which in spite of the best treatment (protection and exercise) there is insufficient strength, a support is necessary. The extent of the paralysis and the weight of the patient determine the type of support to be used. Form-fitting supports are preferable; one may use a jacket of leather and steel or of celluloid, or a corset made of cloth reenforced with stays. With time there is a tendency for fixation of the curvature; this may ultimately be sufficient to permit the patient to discard the support. To hasten the fixation, the fusion operation is of benefit. If the back has not been protected and the curvature is exaggerated, some correction may be taken before the fusion operation is performed; either a Hibbs or an Albee operation may be done, or a graft may be placed in the convexity to act as a supportive column or prop.

The treatment of scoliosis associated with syringomyelia must be directed against the disease itself. Laminectomy with drainage of the cavity fluid has been done, although the use of anesthesia in such cases is dangerous; cervical puncture, exposure of the spinal column to the roentgen rays and the use of mercury and iodides have been tried.

In spastic palsy, treatment of the scoliosis is dependent on the improvement of the hemiplegia and may include correction of the equinus deformity.

In scoliosis due to a deformity elsewhere in the body, for instance a pelvic tilt, correction of the curvature must be directed against the pathologic process which causes the pelvic tilt. If this is a tuberculous hip, the adduction and flexion deformity must be corrected. Frequently a slight raising of the shortened limb will be followed by improvement.

Scoliosis in the dorsal area found in torticollis subsides with correction of the torticollis. If a cast is applied to hold the correction of the head and neck, it may also include an overcorrection of the dorsal area.

For scoliosis due to a destructive lesion of the vertebrae, the treatment is limited to treatment of the lesion itself.

Scoliosis which develops secondary to pleurisy or thoracoplasty cannot be completely corrected, but some improvement is obtained by exercises, particularly deep breathing and the holding of the erect position of the body.

The protective list secondary to sciatica and sacro-iliac disease disappears spontaneously with relief of the primary condition.

The treatment of adolescent scoliosis consists of (1) prophylaxis, (2) correction of the deformity and (3) reestablishment of normal function. Prophylactic treatment necessitates early recognition of an abnormal lateral curvature. Suggestive is the history of fatigue and bad posture in a rapidly growing child. The disrobed child is examined for any increase in the normal curvatures of the vertebral column and the presence of a pelvic tilt. All causative factors are investigated and, whenever possible, eliminated. Strain is relieved by periodic rests; strength is increased by graduated exercises; food deficiencies are replenished by a high caloric diet and, at times, with feeding at intervals. Secondary anemia is treated with iron and liver extract; vitamins are supplied in ample doses, and calcium is added to the diet. The child is encouraged to take part in outdoor activities which include fresh air and sunshine.

If a scoliotic deformity is already present, the curvature must be corrected. The method of correction used is based on the teaching of Professor Haglund.[4] The pelvis is leveled. The dorsal curve is relatively fixed, while the lumbar curve is freely movable and readily corrected. Therefore, in the presence of a right dorsal curvature, if the trunk of the body is made to list to the left, the left lumbar lateral curve is obliterated. In a similar manner, in the presence of kyphosis in the dorsal area the compensatory lumbar lordosis is obliterated by tilting the body forward. Derotation is obtained by fixing the pelvis and rotating the shoulder girdle in the opposite direction, with the arms acting as levers. In this position, if the pelvis is fixed with a plaster of paris jacket which incloses the lumbar area and extends up to the dorsal curve, correction will follow. The body will assume the upright position due to the body-righting reflex. The result will be a correction above the cast in the region of the right dorsal curvature. This correction is controlled by natural forces.

In addition to correcting the deformity, the cast also acts as a support to relieve the functional decompensation. At the same time it permits normal use of the body structures. The patient can pull himself out of the cast and can go on with practically all normal activities. The treatment is entirely ambulatory, permitting the child to go to school.

In early stages full correction can be obtained by this method. To retain the correction it is necessary to reestablish the normal capacity of

4. Haglund, Patrik: Die Entstehung und Behandlung der Skoliosen, Berlin, S. Karger, 1916.

the back. To do this, after the cast has been removed the normal position is held by means of a support, which may be either a steel and leather jacket or a reenforced cloth corset, until the structures have been developed by exercises. The exercises used are graduated physiologic exercises, that is, the carrying out of the normal functions of the back, so that ultimately there is sufficient fixation to give full compensation, which will prevent a recurrence of the deformity.

In cases of severe involvement of long standing, with fixation, it is not possible to obtain complete correction. If the back is compensated, even though the deformity is marked, it is best not to attempt correction, as in breaking down the fixation there is danger of bringing about a decompensation. However, if the patient suffers from pain due to pressure on the nerve, then in spite of the fixation it is necessary to take sufficient correction by the foregoing method to relieve the symptoms.

In order to obtain fixation more rapidly, a fusion operation may be performed. A fusion operation in itself obviously cannot correct the scoliosis. The method most frequently used is the forceful correction by means of turn-buckle casts, followed by a fusion with bone grafts. It has been found that in those cases in which compensation and fixation were obtained after fusion operation, the correction was retained; however, if the decompensation persisted in spite of the bone graft, the deformity continued to increase (Steindler).[5]

The problem of scoliosis is not solved, but with a better understanding of the condition the ultimate outlook for the prevention of a deforming scoliosis is good. This is particularly true of the adolescent type of scoliosis. The answer in the other types of scoliosis lies in the prevention of the disease causing the curvature.

SUMMARY

A new conception of scoliosis is presented. Scoliosis is due, not to an imbalance in the pull of the muscles of the back, as is commonly believed, but to an increase of the normal curvatures of the back. This increase of the normal right dorsal lateral curvature is brought about by a decompensation in the functional capacity of the back. The development of the structural changes is explained. The etiology of adolescent scoliosis is given for the first time and utilized to prescribe prophylactic measures. In addition, a new type of corrective treatment is described. Not only is the deformity improved, but all the secondary disturbances in function are relieved. This method of treatment has been applied successfully over a period of ten years. Owing to the prevalent confusion as to the conception of scoliosis, it was necessary to treat the general consideration of the subject with thoroughness.

5. Steindler, A.: The Compensation Treatment of Scoliosis, J. Bone & Joint Surg. **11**:820-830 (Oct.) 1929.

EFFECT OF CINCHOPHEN ON THE GASTRIC SECRETION

AN EXPERIMENTAL STUDY

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The administration of cinchophen is an effective method for the production of chronic peptic ulcer in dogs. The ulcer thus produced is similar in most respects to the lesion seen in human beings. The ulcer begins as a diffuse gastritis with destruction of the mucosal cells and the formation of multiple erosions throughout the gastric mucosa. These erosions become acute ulcers, which tend to heal. The majority do heal, but one persists as a chronic ulcer, and the gastritis subsides. This chronic lesion is usually situated from 2 to 3 cm. from the pyloric ring on the lesser curvature or on the posterior wall of the stomach. Occasionally, two or more gastric ulcers are present, and there may be an associated duodenal ulcer in a small percentage of the animals. The ulcer readily heals when the administration of cinchophen is stopped.

Many controversial articles have been written on gastric secretion. In general, it is thought that the presence of some free acid in the stomach is necessary for the development of a peptic ulcer. There are reports of peptic ulcer, however, in the presence of achlorhydria, although this occurrence has been contradicted. Whether or not hyperacidity develops in the human stomach before the peptic ulcer forms is not known. There is usually hyperacidity in the presence of peptic ulcer, but this finding is not constant. There is no evidence which demonstrates that a peptic ulcer is more prone to develop in the presence of hyperacidity than it is in the presence of normal acidity. There is hypersecretion in the human stomach during the active stage of peptic ulcer, but it is not known whether this exists prior to the development of the ulcer or not. There are usually hyperacidity and hypersecretion in cases of acute gastritis, and there usually are decreased acidity and hyposecretion in cases of chronic gastritis.

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In view of these findings in the human stomach, we thought that a study of the acidity and the volume of gastric juice secreted during the various phases of development, activity and healing of peptic ulcers which were experimentally produced by the administration of cinchophen would be of interest.

METHODS

Two groups of dogs were used. Both received routine kennel care and were fed a diet composed of cracker crumbs, ground horse meat and evaporated skimmed milk. The food was weighed and fed in sufficient amount to meet the caloric requirements of the animal.

Group 1 consisted of twelve dogs, each of which weighed about 17 Kg. Fractional gastric analysis was performed every second or third day after a fast of twenty-four hours. A large rubber catheter was passed into the stomach, and the residual gastric secretion of the fasting state was removed. One and a half milligrams of histamine phosphate was then given subcutaneously. Each fifteen minutes thereafter the gastric contents were removed. This process was continued until the value for the free acidity returned to the fasting level.

The free and total acidity and the total volume of secretion were determined for each specimen. The free acidity was determined by titrating 2 cc. of filtered gastric contents against a tenth-normal solution of sodium hydroxide, dimethylamino-azobenzene being used as an indicator. The total acidity was determined by a similar titration, with phenolphthalein as an indicator. It was found that there was a consistent difference of never less than 7.5 or more than 12.5 cc. of tenth-normal solution of sodium hydroxide per hundred cubic centimeters of gastric juice between the value for the free and that for the total acidity. Both the free and the total acidity were determined in every specimen, but throughout our results we shall consider only the total acidity.

When a series of five or more fractional analyses had been made with consistent results, the administration of cinchophen was begun. Two grams of this drug, well mixed with the diet, was given daily. The gastric analysis was continued throughout the developmental, the active and the healing stages of ulceration. In many instances, when typical symptoms were present, exploratory laparotomy confirmed the presence of an ulcer. After an ulcer had developed the administration of cinchophen was stopped, but the study of the secretion was continued. All dogs were eventually killed, and necropsy was performed.

Group 2 consisted of five dogs, each of which weighed about 12 Kg. Each dog had a fundic pouch. These pouches were made from the greater curvature of the stomach. The splenic vessels attached to the fundus were kept intact, and the pouch was left in the abdominal cavity. The contents, which were collected continuously, drained through a de Pezzer catheter into a balloon carried in a basket on the side of the dog. No animals were used that had any leakage around the catheter.

The animals were fed the weighed amount of food daily at 8:30 a. m. The balloon was emptied daily at 8:30 a. m., 12:30 p. m., 4:30 p. m. and 10 p. m. The secretion was collected for ten or more days after complete healing of the operative wound, and a constant normal was established before cinchophen was given. Cinchophen in doses varying from 0.25 to 2 Gm. daily was then mixed

with the diet, and the same observations were continued. Administration of this drug was continued until the dog died or was killed.

RESULTS

Group 1.—The results obtained from the study of the twelve dogs in group 1 can best be described in a general way as they were identical, or nearly so, in every case. After the subcutaneous injection of histamine, the fasting value for the total gastric acidity, which normally varies from 0 to 40 according to the method of Töpfer, rose to between 100 and 150. This rise usually occurred within the first fifteen minutes, but it always occurred by the end of thirty minutes. There was then a progressive decrease in the value for the total acidity, until at the end of from sixty to ninety minutes the fasting level had been reached.

The volume output of gastric juice fluctuated in direct proportion to the acidity. This output, which varied with the animal, averaged from 100 to 150 cc. during the course of a histamine curve. From 2 to 5 cc. of gastric juice was obtained from the fasting dog. From 30 to 50 cc. was usually obtained at the peak of the acid curve. This amount decreased simultaneously with the acid to the original fasting volume.

A chronic gastric ulcer developed in eleven of the twelve dogs in an average of eighteen days after the administration of cinchophen had been commenced. The twelfth dog received cinchophen for sixty days; at necropsy a grossly normal stomach was found. There was no change at any time in the gastric acidity or volume secretion of gastric juice in this dog.

After the administration of cinchophen, no change was noted in the gastric acidity of the eleven dogs in which ulcers developed. The secretory curve of four of the dogs was prolonged for from thirty to sixty minutes; that is, it required from thirty to sixty minutes more time for the gastric acidity to return to the original fasting level. This occurred after the dog manifested some symptoms of a peptic ulcer and disappeared when the administration of cinchophen was stopped and the ulcer healed.

There was a consistent demonstrable change in the volume output of gastric juice in every case. After the administration of cinchophen, there was no significant change until such symptoms of early gastritis, such as tarry stools and occasional vomiting of small amounts of gastric contents, were present. This change occurred as early as the third day and as late as the twentieth day after the initial dose of the drug had been administered and increased with the development of gastritis. The amount of increased gastric secretion varied from 75 to 200 cc. There was no change in the gross appearance of the gastric contents, such as visible blood, that would account for this increase in the amount of secretion.

When the administration of cinchophen was discontinued there was a gradual decrease of the amount of gastric secretion to the normal level within two weeks. The results obtained with dog A were typical (chart 1). The administration of cinchophen was begun on the eighth day of the study, and on the twentieth day the stools were tarry. Three days later there was marked hypersecretion, which continued. Exploratory laparotomy revealed a gastric ulcer. The administration of the drug was then discontinued and the volume output of gastric juice returned to normal as the ulcer healed.

The symptoms of ulcer were most marked coincident with the largest amount of gastric secretion, and it was at this time that an exploratory laparotomy was generally done. If the administration of cinchophen was continued, the volume output of gastric juice gradually diminished until a definite hyposecretion was present. Within from five to ten days the amount of secretion returned to the normal level or slightly below normal, and after another two weeks it was from 25 to 50 per cent below normal.

This finding is illustrated in part by dog B, which was given 2 Gm. of cinchophen daily. The average normal volume output of gastric juice was 137 cc. A diagnosis of ulcer was made when an average volume of secretion of 257 cc. of gastric juice had been reached. The administration of cinchophen was continued, but there was a gradual decrease in the output of gastric juice, until on the twelfth day of administration there was an average of only 125 cc. The dog was then killed, and a perforating gastric ulcer was found to be present.

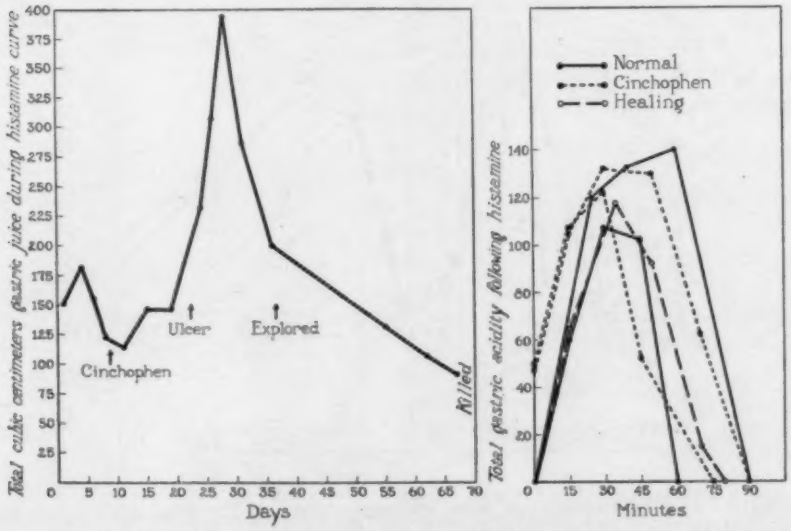

Chart 1.—Total volume output of gastric juice during the different phases of the experiment and total gastric acidity (phenolphthalein indicator) after stimulation with histamine. Daily administration of 2 Gm. of cinchophen was begun on the eighth day and continued to the time of exploration.

Group 2.—The results obtained from observation of the five dogs with fundic pouches confirmed for the most part the results obtained in group 1. The average daily output of gastric juice from the pouches was approximately from 125 to 150 cc. The fasting value for the total gastric acidity varied from 0 to 20. The value for the acidity increased from 8:30 a. m., at which time the dogs were fed, to 12:30 p. m., at which time it varied between 130 and 150, where it remained with only a slight increase until 4:30 p. m. There was then a steady decrease, and at 10 p. m. the average value for the acidity varied from 50 to 75, and by 8 a. m. the fasting level was again reached. The maximal volume output of gastric juice occurred at the time of the greatest acidity, which was at 4:30 p. m.

A peptic ulcer developed in the pouches of all five dogs. When the dose of cinchophen was 1 Gm. or more daily, the ulcers developed in from two to five days and usually perforated. The process was the same as that seen in the intact stomach. In every case the administration of 0.5 Gm. or more of the drug caused evidence of gastritis within eight hours after the initial dose. There was macroscopic evidence of bleeding from the pouches between the fourth and the twelfth hour each day. When a definite ulcer was present this bleeding was so marked in a few cases that the study of the secretion was discontinued. No results have been recorded in which the presence of blood may have been a complicating factor.

The administration of from 0.25 to 2 Gm. of cinchophen daily had no significant effect on the height of the acidity curve. There was, however, the same prolongation of the curve as seen in group 1.

Dog C revealed the typical volume output of gastric juice (chart 2). A normal daily average of 153 cc. was established. One gram of cinchophen was given at

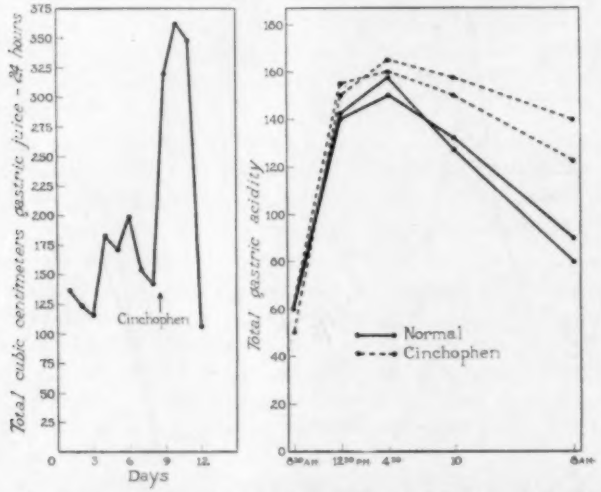

Chart 2.—Total twenty-four hour volume output and the total acidity (phenolphthalein indicator) of the secretion of the fundic pouch of dog C. One gram of cinchophen was administered daily; the dog died of a perforated ulcer of the pouch.

8:30 a. m. At 4:30 p. m. on the same day there was an increase of more than 50 cc. in the volume output. This increase persisted, and the total volume output for the day was 320 cc., or more than twice the amount secreted before the administration of the drug. This hypersecretion continued for seventy-two hours; hyposecretion then developed, and only 100 cc. was secreted. The dog died on the following day as a result of a hemorrhage from a perforated ulcer in the pouch.

Dog D (chart 3) was given 2 Gm. of cinchophen daily. A normal output of 119 cc. of gastric juice per day was established. Eight hours after the initial dose of the drug, the volume output of gastric juice was increased 100 per cent. The total output in twenty-four hours was 203 cc., or nearly 75 per cent more than normal. The following two days the volume output was less than normal. The dog was killed, and a perforated ulcer was found in the pouch.

Dog E was given 0.25 Gm. of cinchophen daily. An average normal output of 209 cc. of gastric juice was established. A definite hypersecretion began during the second twenty-four hours after the administration of cinchophen and persisted for seven days. A maximal output of 323 cc. was reached, and a daily average of 279 cc. was maintained. The dog remained well and had no bleeding during this period.

On the eighth day, 0.5 Gm. of cinchophen was given; bleeding began, and the daily output of gastric juice decreased to 158 cc. One gram of the drug was then given. The bleeding became more marked, and an ulcer developed. Concomitantly, the volume output decreased to from 110 to 122 cc. The dog was killed because of a hemorrhage from the pouch. There were three ulcers, varying from acute to subacute, in the pouch.

The remaining two dogs were given doses of cinchophen varying from 0.5 to 2.5 Gm. The results were similar to those previously described.

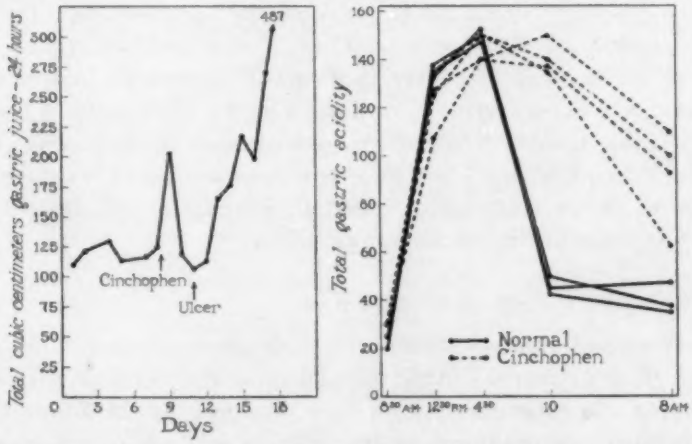

Chart 3.—Total twenty-four hour volume output and the acidity (phenolphthalein indicator) of the secretion of the fundic pouch of dog D. Two grams of cinchophen was administered daily; the increase in the volume of gastric juice after the formation of an ulcer was caused by hemorrhage. Prolongation of the acidity curve may be noted.

COMMENT

These results agree in several respects with the usual findings of the gastric secretion in the presence of gastritis and peptic ulcer in man. The results in group 1 and group 2 nearly parallel each other. With the initial damage of the mucosal cells there is an increase in the amount of gastric secretion, but as more cells are damaged and a definite ulcer occurs, there is a decrease in the amount of secretion. This decrease may be the result of a toxic inhibition of the secreting cells.

In all probability the secretion of the pouches, which was determined, was comparable to the secretion occurring in the stomach proper. The ulcerative process was more rapid in the pouches because of the constant

presence of free acid. A longer study would have been desirable, but the rapidity with which ulcer developed in the isolated gastric pouch and the high incidence of perforation prevented prolonged observations. The amount of bleeding interfered in some cases with the study, but in no case could it be considered a factor in the results.

The ulcer developed during the stage of hypersecretion and was always present at the time of maximal volume output. The increased amount of secretion and consequently a relative increase in the degree of acidity was undoubtedly an important factor in the production of the peptic ulcer from the initial mucosal erosion. The fact that there was no change in the gastric secretion of the one dog in which a peptic ulcer did not develop is at least suggestive.

The action of cinchophen on the gastric secretion is the same as might be expected from a toxin. It is usually accepted that a toxin first stimulates and then depresses. Dog E demonstrates this. When 0.25 Gm. of the drug was given there was a continuous hypersecretion. This dose was not sufficient to produce a peptic ulcer and did not cause any noticeable toxicity. When the toxic dose of 0.5 Gm. was given, a peptic ulcer rapidly developed and there was a marked decrease in the amount of gastric secretion. A further increase in the dose caused a further decrease in the volume of secretion.

SUMMARY

The free and total acidity and the total volume output of the gastric contents were measured during the phases of the development, activity and healing of peptic ulcer which were produced by the administration of cinchophen. A fractional gastric analysis was performed on twelve dogs. The secretion was collected from five fundic pouches at definite intervals throughout the day and night. The results were comparable in the two groups. After the administration of variable doses of cinchophen, there was no change in the level of acidity, but there was an increase in the amount of gastric secretion. This initial hypersecretion was followed by the development of a peptic ulcer and hyposecretion.

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